APPLICATION

for

UNITED STATES LETTERS PATENT

on

1,2-DISUBSTITUTED-6-OXO-3-PHENYL-PIPERIDINE-3-CARBOXAMIDES AND COMBINATORIAL LIBRARIES THEREOF

By

Jeffrey D. KAHL
Normand HEBERT

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Attorneys
ARENT FOX KINTNER PLOTKIN & KAHN, PLLC
1050 Connecticut Avenue, N.W. Suite 400
Washington, D.C. 20036
Customer No. 004372

1,2-DISUBSTITUTED-6-OXO-3-PHENYL-PIPERIDINE-3-CARBOXAMIDES.

AND COMBINATORIAL LIBRARIES THEREOF

FIELD OF THE INVENTION

[0001] The present invention relates generally to the synthesis of compounds comprising piperidine-3-carboxamides. In one embodiment, the invention provides novel 1,2-disubstituted-6-oxo-3-phenyl-piperidine-3-carboxamide derivative compounds as well as novel combinatorial libraries comprised of such compounds.

BACKGROUND INFORMATION

[0002] The process of discovering new therapeutically active compounds for a given indication involves the screening of all compounds from available compound collections. From the compounds tested, one or more structures are selected as a promising lead. A large number of related analogs are then synthesized in order to develop a structure-activity relationship and select one or more optimal compounds. With traditional "one-at-a-time" synthesis and biological testing of analogs, this optimization process is long and labor intensive. Adding significant numbers of new structures to the compound collections used in the initial screening step of the discovery and optimization process cannot be accomplished with traditional "one-at-a-time" synthesis methods, except over a time frame of years or even decades. Faster methods are needed that allow for the preparation of up to thousands of related compounds in a matter of days or a few weeks. This need is particularly evident when it comes to synthesizing more complex compounds, such as piperidine-3-carboxamide derivative compounds.

[0003] Combinatorial approaches have been extended to "organic," or non-peptide, libraries. However, the libraries to date contain compounds of limited

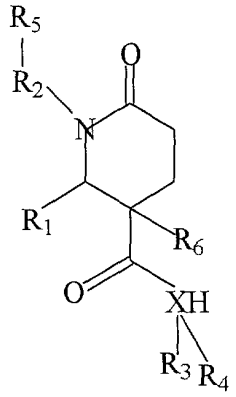
diversity and complexity. A need therefore exists to develop more complex libraries based on medicinal compounds which would need less time and effort in the synthesis and testing required to bring an organic pharmaceutical product to fruition. In short, improved methods for generating therapeutically useful compounds, such as piperidine-3-carboxamide derivatives, are desired.

[0004] Piperidine and carboxamide derivative compounds have been the subject of investigation in a number of different biological areas. For example, piperidine-3-carboxamides have been proposed or used as platelet aggregation inhibitors (Zheng, et al., "Design and synthesis of piperidine-3-carboxamides as human platelet aggregation inhibitor", (1995), Journal of Medicinal Chemistry, vol. 38, No. 1, pp. 180-188) and piperidine derivatives have been proposed as medicaments with rennin inhibiting activity (U.S. Patent No. 6,150,526 issued on November 21, 2000 and U. S. Patent No. 6,051,712 issued on April 18, 2000 both by to Binggeli, et al.)

[0005] This invention satisfies the above discussed need and provides related advantages as well. The present invention overcomes the known limitations to classical serial organic synthesis of piperidine-3-carboxamide derivatives, for example, as well as the shortcomings of combinatorial chemistry related to piperidine-3-carboxamide derivatives. The present invention allows for rapid generation of large diverse libraries of complex piperidine-3-carboxamide derivatives as discrete molecules. The present invention can utilize a readily available pool of building blocks that can be incorporated into the various regions of the molecule. Furthermore, the method of making the present invention allows for the use of building blocks that contain a wide range of diverse functionality. Such building blocks can provide combinatorial libraries that consist of large numbers as well as combinatorial libraries that are extremely diverse with respect to the functionality contained within those libraries. The present invention combines the techniques of solid-phase synthesis of piperidine-3-carboxamide derivatives and the general techniques of synthesis of combinatorial libraries to prepare highly diverse new piperidine-3-carboxamide derivative compounds.

SUMMARY OF THE INVENTION

[0006] The present invention relates to novel piperidine-3-carboxamide derivative compounds of the following formula:



wherein

[0007] X is selected from the group consisting of N and O;

[0008] R_1 is selected from the group consisting of a substituted aromatic heterocyclic ring, C_3-C_{12} substituted alicycle and substituted phenyl;

[0009] R_2 is selected from the group consisting of H; -OH; C_1 to C_7 alkoxy; C_1 to C_7 substituted alkoxy; C_2-C_7 alkenyl; C_1 to C_7 substituted alkenyl; C_2 to C_7 alkynyl; C_2 to C_7 substituted alkynyl; unsubstituted phenyl; naphthyl; substituted phenoxy; C_2 to C_7 heterocyclic ring; substituted C_2 to C_7 heterocyclic ring; substituted cyclic C_2 to C_7 alkylene; C_1 to C_7 alkyl; C_1 to C_7 substituted alkyl; C_3 to C_7 cycloalkyl; C_3 to C_7 substituted cycloalkyl; C_1 to C_7 alkoxy; halo; C_1 to C_{10} alkylthio; C_1 to C_{10} substituted alkylthio; C_1 to C_{10} alkylnitrile; a C_7 to C_{18} substituted phenylalkyl; substituted phenyl;

[0010] R_3 and R_4 are independently selected from the group consisting of –OH; H; C_1 to C_6 alkyl; C_1 to C_7 substituted alkyl; C_2 to C_7 alkenyl; C_1 to C_7 alkoxy; C_1 to C_7 substituted alkoxy; C_3 to C_7 cycloalkyl; C_3 to C_7 substituted cycloalkyl; C_1

to C_{10} alkylthio; C_1 to C_{10} alkylnitrile; C_1 to C_4 alcohol; substituted phenyl; C_1 to C_6 substituted alkyl; C_1 to C_7 alkoxy; C_3 to C_7 cycloalkyl; and C_3 to C_7 substituted cycloalkyl; C_2 to C_7 heterocyclic ring; C_2 to C_7 substituted heterocyclic ring; phenoxy; and substituted phenoxy,

[0011] R_5 is selected from the group consisting of H and NH_2, and

[0012] R_6 is selected from the group consisting of phenyl, substituted phenyl, C_2 to C_7 heterocyclic ring, and substituted C_2 to C_7 heterocyclic ring.

[0013] The invention further relates to combinatorial libraries containing two or more such compounds, as well as methods of preparing piperidine-3-carboxamide derivative compounds.

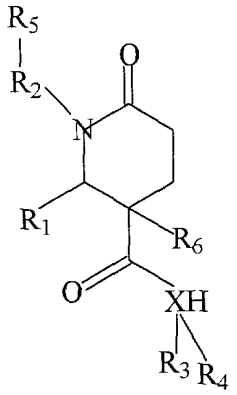
BRIEF DESCRIPTION OF THE DRAWING

[0014] Figures 1 and 2 show two parts of a scheme for the combinatorial synthesis of piperidine-3-carboxamide derivative compounds.

[0015] Figure 3 shows a scheme for the production of (Substituted Phenyl)-glutaric anhydrides.

DETAILED DESCRIPTION OF THE INVENTION

[0016] The present invention provides compounds and combinatorial libraries of compounds of the formula:



wherein:

[0017] X is selected from the group consisting of N and O;

[0018] R_1 is selected from the group consisting of a substituted aromatic heterocyclic ring, C_3-C_{12} substituted alicycle and substituted phenyl;

[0019] R_2 is selected from the group consisting of H; -OH; C_1 to C_7 alkoxy; C_1 to C_7 substituted alkoxy; C_2-C_7 alkenyl; C_1 to C_7 substituted alkenyl; C_2 to C_7 alkynyl; C_2 to C_7 substituted alkynyl; unsubstituted phenyl; naphthyl; substituted phenoxy; C_2 to C_7 heterocyclic ring; substituted C_2 to C_7 heterocyclic ring; substituted cyclic C_2 to C_7 alkylene; C_1 to C_7 alkyl; C_1 to C_7 substituted alkyl; C_3 to C_7 cycloalkyl; C_3 to C_7 substituted cycloalkyl; C_1 to C_7 alkoxy; halo; C_1 to C_{10} alkylthio; C_1 to C_{10} substituted alkylthio; C_1 to C_{10} alkylnitrile; a C_7 to C_{18} substituted phenylalkyl; substituted phenyl;

[0020] R_3 and R_4 are independently selected from the group consisting of –OH; H; C_1 to C_6 alkyl; C_1 to C_7 substituted alkyl; C_2 to C_7 alkenyl; C_1 to C_7 alkoxy; C_1 to C_7 substituted alkoxy; C_3 to C_7 cycloalkyl; C_3 to C_7 substituted cycloalkyl; C_1 to C_{10} alkylthio; C_1 to C_{10} alkylnitrile; C_1 to C_4 alcohol; substituted phenyl; C_1 to C_6 substituted alkyl; C_1 to C_7 alkoxy; C_3 to C_7 cycloalkyl; and C_3 to C_7 substituted cycloalkyl; C_2 to C_7 heterocyclic ring; C_2 to C_7 substituted heterocyclic ring; phenoxy; and substituted phenoxy,

[0021] R_5 is selected from the group consisting of H and NH_2, and

[0022] R_6 is selected from the group consisting of phenyl, substituted phenyl, C_2 to C_7 heterocyclic ring, and substituted C_2 to C_7 heterocyclic ring.

[0023] The invention also provides methods of preparing piperidine-3-carboxamide derivative compounds and combinatorial libraries. In one method, as shown in Figures 1 and 2, such compounds can be prepared by a process comprising:

[0024] preparing a resin bound aldehyde or diamine,

[0025] reacting said resin bound aldehyde with an amine, or said resin bound diamine with an aldehyde, to form a resin bound imine,

[0026] cyclizing said resin bound imine to produce a resin bound carboxylic acid,

[0027] acylating said resin bound carboxylic acid, and

[0028] cleaving and extracting said piperidine-3-carboxamide derivative compound from said resin.

[0029] Examples of aldehydes which are useful in the above reaction include but are not limited to 4-hydroxybenzaldehyde, 3-hydroxybenzaldehyde, 2-hydroxy-5-methylbenzaldehyde, 3,5-dimethyl-4-hydroxybenzaldehyde, 2-hydroxy-4-methoxybenzaldehyde, 3-ethoxysalicylaldehyde, 2-hydroxy-1-naphthaldehyde, 5-bromosalicylaldehyde, cyclopropanecarboxaldehyde, 3-furaldehyde, benzaldehyde, 2-thiophenecarboxaldehyde, 3-thiophenecarboxaldehyde, P-tolualdehyde, 4,5-dimethyl-2-furancarboxaldehyde, P-anisaldehyde, 5-methylfurfural, O-tolualdehyde, 2,4,5-trimethylbenzaldehyde, piperonal, 5-methyl-2-thiophenecarboxaldehyde, 4-(difluoromethyoxy)benzaldehyde, 5-bromo-2-furaldehyde, 4-biphenylcarboxaldehyde and 5-bromo-2-thiophenecarboxaldehyde.

[0030] Examples of diamines and amines useful in the above reaction when producing a resin bound diamine or reaction an aldehyde with an amine, include but are not limited to methylamine, ethylamine, propargylamine, cyclopropylamine, allylamine, propylamine, 3-aminopropionitrile, isobutylamine, cyclopentylamine, cyclohexylamine, hexylamine, N-acetylethylenediamine, 3-ethoxypropylamine, 4-chlorobenzylamine, 1-(3-aminopropyl)-2-pyrrolidinone, tryptamine, 3-(trifluoromethyl)benzylamine, 2,4-diclorophenethylamine, 4-amino-1-benzylpiperidine, benzylamine, ethylenediamine, 1,3-diaminopropane, 1,4-diaminobutane, trans-1,2-cyclohexanediamine, trans-1,4-diaminocyclohexane, 2,2-thiobis(ethylamine), and N,N-Bis(3-aminopropyl)methylamine.

[0031] Examples of amines useful in the above reaction when acylating the resin bound carboxylic acid include but are not limited to nipecotamide, 1-(2-aminoethyl)pyrrolidine, pyrrolidine, histamine, cyclopentylamine, allylamine, 2-methoxyethylamine, cyclohexylamine, 1-methylpiperazine, tetrahydrofurfurylamine, 4-methylbenzylamine, 3-fluorobenzylamine, 4-fluorobenzylamine, 1-(3-aminopropyl)imidazole, cyclopropylamine, propylamine, ethanolamine, 2-thiophenemethylamine, n,n-dimethyl-1,3-propanediamine, 1-(2-

aminoethyl)piperidine, isoamylamine, 3-ethoxypropylamine, (r)-(-)-1-cyclohexylethylamine, neopentylamine, 3-(methylthio)propylamine, isobutylamine, 3-amino-1-propanol, 2-ethoxyethylamine, 2,6-dimethylpiperazine, propargylamine, thiophene-2-ethylamine, butylamine, 2-amino-1-methoxypropane, 3-aminopropionitrile, 3-methylpiperidine, P-anisidine, 1,2,3,6-tetrahydropyridine, 2,6-dimethylmorpholine, methoxyamine hydrochloride, n-ethylpiperazine, water, and hydroxylamine.

[0032] When the above-described compounds include one or more chiral centers, the stereochemistry of such chiral centers can independently be in the R or S configuration, or a mixture of the two. The chiral centers can be further designated as R or S or R,S or d,D, l,L or d,l, D,L.

[0033] In the above formula , the term "C_1 to C_7 alkyl" denotes such radicals as methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, amyl, tert-amyl, hexyl and the like. The preferred "C_1 to C_7 alkyl" groups are methyl, iso-butyl, sec-butyl and iso-propyl.

[0034] The term "C_1 to C_7 substituted alkyl," denotes that the above C_1 to C_7 alkyl groups are substituted by one or more, and preferably one or two, halogen, hydroxy, protected hydroxy, oxo, protected oxo, C_3 to C_7 cycloalkyl, naphthyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, imidazolyl, indolyl, pyrrolidinyl, C_1 to C_7 alkoxy, C_1 to C_7 acyl, C_1 to C_7 acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N,N-di(C_1 to C_6 alkyl)carboxamide, cyano, methylsulfonylamino, thiol, C_1 to C_4 alkylthio or C_1 to C_4 alkylsulfonyl groups. The substituted alkyl groups may be substituted once or more, and preferably once or twice, with the same or with different substituents.

[0035] Examples of the above substituted alkyl groups include the 2-oxo-prop-1-yl, 3-oxo-but-1-yl, cyanomethyl, nitromethyl, chloromethyl, hydroxymethyl, tetrahydropyranyloxymethyl, trityloxymethyl, propionyloxymethyl, amino, methylamino, aminomethyl, dimethylamino, carboxymethyl,

allyloxycarbonylmethyl, allyloxycarbonylaminomethyl, methoxymethyl, ethoxymethyl, t-butoxymethyl, acetoxymethyl, chloromethyl, bromomethyl, iodomethyl, trifluoromethyl, 6-hydroxyhexyl, 2,4-dichloro(n-butyl), 2-aminopropyl, 1-chloroethyl, 2-chloroethyl, 1- bromoethyl, 2-chloroethyl, 1-fluoroethyl, 2-fluoroethyl, 1- iodoethyl, 2-iodoethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, 1-bromopropyl, 2-bromopropyl, 3-bromopropyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, 1- iodopropyl, 2-iodopropyl, 3-iodopropyl, 2-aminoethyl, 1- aminoethyl, N-benzoyl-2-aminoethyl, N-acetyl-2-aminoethyl, N-benzoyl-1-aminoethyl, N-acetyl-1-aminoethyl and the like.

[0036] The term "C_1 to C_7 alkoxy" as used herein denotes groups such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, t-butoxy and like groups. A preferred alkoxy is methoxy. The term "C_1 to C_7 substituted alkoxy" means the alkyl portion of the alkoxy can be substituted in the same manner as in relation to C_1 to C_7 substituted alkyl. Similalry, the term "C_1 to C_7 phenylalkoxy" as used herein means "C_1 to C_7 alkoxy" bonded to a phenyl radical.

[0037] The substituent term "C_3 to C_7 cycloalkyl" includes the cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl rings. The substituent term "C_3 to C_7 substituted cycloalkyl" indicates the above cycloalkyl rings substituted by one or two halogen, hydroxy, protected hydroxy, C_1 to C_4 alkylthio, C_1 to C_4 alkylsulfoxide, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylthio, C_1 to C_4 substituted alkylsulfoxide, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, oxo, protected oxo, (monosubstituted)amino, (disubstituted)amino, trifluoromethyl, carboxy, protected carboxy, phenyl, substituted phenyl, phenylthio, phenylsulfoxide, phenylsulfonyl, amino, or protected amino groups.

[0038] The term "substituted phenyl" specifies a phenyl group substituted with one or more, and preferably one or two, moieties chosen from the groups consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, C_1 to C_7 substituted alkoxy, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_1 to C_7 alkylthio, C_1 to C_7 acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected

hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N, N-di(C_1 to C_6 alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_6 alkyl)sulfonyl)amino, - (phenylsulfonyl)amino or phenyl, wherein the phenyl is substituted or unsubstituted, such that, for example, a biphenyl results.

[0039] Examples of the term "substituted phenyl" includes a mono- or di(halo)phenyl group such as 2, 3 or 4-chlorophenyl, 2,6-dichlorophenyl, 2,5-dichlorophenyl, 3,4-dichlorophenyl, 2, 3 or 4-bromophenyl, 3,4-dibromophenyl, 3-chloro-4-fluorophenyl, 2, 3 or 4-fluorophenyl and the like; a mono or di(hydroxy)phenyl group such as 2, 3 or 4-hydroxyphenyl, 2,4-dihydroxyphenyl, the protected-hydroxy derivatives thereof and the like; a nitrophenyl group such as 2, 3 or 4-nitrophenyl; a cyanophenyl group, for example, 2, 3 or 4-cyanophenyl; a mono- or di(alkyl)phenyl group such as 2, 3 or 4-methylphenyl, 2,4-dimethylphenyl, 2, 3 or 4-(iso-propyl)phenyl, 2, 3 or 4-ethylphenyl, 2, 3 or 4-(n-propyl)phenyl and the like; a mono or di(alkoxyl)phenyl group, for example, 2,6-dimethoxyphenyl, 2, 3 or 4-methoxyphenyl, 2, 3 or 4-ethoxyphenyl, 2, 3 or 4-(isopropoxy)phenyl, 2, 3 or 4-(t-butoxy)phenyl, 3-ethoxy-4-methoxyphenyl and the like; 2, 3 or 4-trifluoromethylphenyl; a mono- or dicarboxyphenyl or (protected carboxy)phenyl group such as 2, 3 or 4-carboxyphenyl or 2,4-di(protected carboxy)phenyl; a mono-or di(hydroxymethyl)phenyl or (protected hydroxymethyl)phenyl such as 2, 3, or 4-(protected hydroxymethyl)phenyl or 3,4-di(hydroxymethyl)phenyl; a mono- or di(aminomethyl)phenyl or (protected aminomethyl)phenyl such as 2, 3 or 4-(aminomethyl)phenyl or 2,4-(protected aminomethyl)phenyl; or a mono- or di(N-(methylsulfonylamino))phenyl such as 2, 3 or 4-(N-(methylsulfonylamino))phenyl. Also, the term "substituted phenyl" represents disubstituted phenyl groups wherein the substituents are different, for example, 3-methyl-4-hydroxyphenyl, 3-chloro-4-hydroxyphenyl, 2-methoxy-4-bromophenyl, 4-ethyl-2-hydroxyphenyl, 3-hydroxy-4-nitrophenyl, 2-hydroxy 4-chlorophenyl and the like.

[0040] The terms "halo" and "halogen" refer to the fluoro, chloro, bromo or

iodo atoms. There can be one or more halogen, which are the same or different. Preferred halogens are chloro and fluoro.

[0041] The term "substituted amino" refers to an amino group with one substituent chosen from the group consisting of phenyl, substituted phenyl, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_2 to C_7 alkenyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 alkynyl, C_2 to C_7 substituted alkynyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl and heterocyclic ring. The substituted amino can additionally have an amino-protecting group as encompassed by the term "protected substituted amino."

[0042] The term "(disubstituted)amino" refers to an amino group with two substituents chosen from the group consisting of phenyl, substituted phenyl, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 acyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_7 to C_{12} phenylalkyl, and C_7 to C_{12} substituted phenylalkyl. The two substituents can be the same or different.

[0043] The term "C_1 to C_4 alkylthio" refers to sulfide groups such as methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, t-butylthio and like groups.

[0044] The term "C_1 to C_4 substituted alkylthio," denotes that the C_1 to C_4 alkyl portion of this group may be substituted as described above in relation to "substituted alkyl."

[0045] The term "phenoxy" denotes a phenyl bonded to an oxygen atom, wherein the binding to the rest of the molecule is through the oxygen atom. The term "substituted phenoxy" specifies a phenoxy group substituted with one or more, and preferably one or two, moieties chosen from the groups consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_{12} alkyl, C_1 to C_{12} alkoxy, C_1 to C_{12} substituted alkoxy, C_1 to C_{12} acyl, C_1 to C_{12} acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C_1 to C_{12} alkyl)carboxamide, protected N-(C_1 to C_{12} alkyl)carboxamide, N, N-di(C_1 to C_{12} alkyl)carboxamide, trifluoromethyl, N-((C_1 to

C_{12} alkyl)sulfonyl)amino and N- (phenylsulfonyl)amino.

[0046] The terms "C_7 to C_{18} substituted phenylalkyl" and "C_1 to C_{12} substituted heterocycloalkyl" denote a C_7 to C_{18} phenylalkyl group or C_1 to C_{12} heterocycloalkyl substituted (on the alkyl or, where applicable, phenyl or heterocyclic portion) with one or more, and preferably one or two, groups chosen from halogen, hydroxy, protected hydroxy, oxo, protected oxo, amino, protected amino, substituted amino, protected substituted amino, (disubstituted)amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, C_1 to C_{12} alkyl, C_1 to C_{12} substituted alkyl, C_1 to C_{12} alkoxy, C_1 to C_{12} substituted alkoxy, C_1 to C_{12} acyl, C_1 to C_{12} substituted acyl, C_1 to C_{12} acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C_1 to C_{12} alkyl)carboxamide, protected N-(C_1 to C_{12} alkyl)carboxamide, N, N-(C_1 to C_{12} dialkyl)carboxamide, cyano, N-(C_1 to C_{12} alkylsulfonyl)amino, thiol, C_1 to C_{10} alkylthio, C_1 to C_{10} alkylsulfonyl groups; and/or the phenyl group may be substituted with one or more, and preferably one or two, substituents chosen from halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_{12} alkyl, C_1 to C_{12} substituted alkyl, C_1 to C_{12} alkoxy, C_1 to C_{12} substituted alkoxy, C_1 to C_{12} acyl, C_1 to C_{12} substituted acyl, C_1 to C_{12} acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C_1 to C_{12} alkyl)carboxamide, protected N-(C_1 to C_{12} alkyl)carboxamide, N, N-di(C_1 to C_{12} alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_{12} alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino, cyclic C_2 to C_{12} alkylene or a phenyl group, substituted or unsubstituted, for a resulting biphenyl group. The substituted alkyl, phenyl or heterocyclic groups may be substituted with one or more, and preferably one or two, substituents which can be the same or different.

[0047] Examples of the term "C_7 to C_{18} substituted phenylalkyl" include groups such as 2-phenyl-1-chloroethyl, 2-(4-methoxyphenyl)ethyl, 4-(2,6-dihydroxy phenyl)n-hexyl, 2-(5-cyano-3-methoxyphenyl)n-pentyl, 3-(2,6-dimethylphenyl)n-propyl, 4-chloro-3-aminobenzyl, 6-(4-methoxyphenyl)-3-carboxy(n-hexyl), 5-(4-

aminomethylphenyl)- 3-(aminomethyl)n-pentyl, 5-phenyl-3-oxo-n-pent-1-yl and the like.

[0048] The term "C_7 to C_{18} phenylalkylene" specifies a C_7 to C_{18} phenylalkyl, as defined above, where the phenylalkyl radical is bonded at two different positions connecting together two separate additional groups. The definition includes groups of the formula: -phenyl-alkyl-, -alkyl-phenyl- and -alkyl-phenyl-alkyl-. Substitutions on the phenyl ring can be 1,2, 1,3 or 1,4.

[0049] C_7 to C_{18} phenylalkylenes include, for example, 1,4-tolylene and 1,3-xylylene.

[0050] The terms "cyclic C_2 to C_7 alkylene," "substituted cyclic C_2 to C_7 alkylene," "cyclic C_2 to C_7 heteroalkylene," and "substituted cyclic C_2 to C_7 heteroalkylene," defines such a cyclic group bonded ("fused") to the phenyl radical resulting in a bicyclic ring system. The cyclic group may be saturated or contain one or two double bonds. Furthermore, the cyclic group may have one or two methylene or methine groups replaced by one or two oxygen, nitrogen or sulfur atoms which are the cyclic C_2 to C_7 heteroalkylene.

[0051] The cyclic alkylene or heteroalkylene group may be substituted once or twice by the same or different substituents which, if appropriate, can be connected to another part of the compound (e.g., alkylene) selected from the group consisting of the following moieties: hydroxy, protected hydroxy, carboxy, protected carboxy, oxo, protected oxo, C_1 to C_4 acyloxy, formyl, C_1 to C_{12} acyl, C_1 to C_{12} alkyl, C_1 to C_7 alkoxy, C_1 to C_{10} alkylthio, C_1 to C_{10} alkylsulfoxide, C_1 to C_{10} alkylsulfonyl, halo, amino, protected amino, substituted amino, protected substituted amino, (disubstituted)amino, hydroxymethyl or a protected hydroxymethyl.

[0052] The cyclic alkylene or heteroalkylene group fused onto the benzene radical can contain two to ten ring members, but it preferably contains three to six members. Examples of such saturated cyclic groups are when the resultant bicyclic ring system is 2,3-dihydro-indanyl and a tetralin ring. When the cyclic groups are unsaturated, examples occur when the resultant bicyclic ring system is a naphthyl ring or indolyl. Examples of fused cyclic groups which each contain

one nitrogen atom and one or more double bond, preferably one or two double bonds, are when the benzene radical is fused to a pyridino, pyrano, pyrrolo, pyridinyl, dihydropyrrolo, or dihydropyridinyl ring. Examples of fused cyclic groups which each contain one oxygen atom and one or two double bonds are when the benzene radical ring is fused to a furo, pyrano, dihydrofurano, or dihydropyrano ring. Examples of fused cyclic groups which each have one sulfur atom and contain one or two double bonds are when the benzene radical is fused to a thieno, thiopyrano, dihydrothieno or dihydrothiopyrano ring. Examples of cyclic groups which contain two heteroatoms selected from sulfur and nitrogen and one or two double bonds are when the benzene radical ring is fused to a thiazolo, isothiazolo, dihydrothiazolo or dihydroisothiazolo ring. Examples of cyclic groups which contain two heteroatoms selected from oxygen and nitrogen and one or two double bonds are when the benzene ring is fused to an oxazolo, isoxazolo, dihydrooxazolo or dihydroisoxazolo ring. Examples of cyclic groups which contain two nitrogen heteroatoms and one or two double bonds occur when the benzene ring is fused to a pyrazolo, imidazolo, dihydropyrazolo or dihydroimidazolo ring or pyrazinyl.

[0053] The term "heterocycle" or "heterocyclic ring" denotes optionally substituted five-membered to eight-membered rings that have 1 to 4 heteroatoms, such as oxygen, sulfur and/or nitrogen, in particular nitrogen, either alone or in conjunction with sulfur or oxygen ring atoms. These five-membered to eight-membered rings may be saturated, fully unsaturated or partially unsaturated, with fully saturated rings being preferred. Preferred heterocyclic rings include morpholino, piperidinyl, piperazinyl, 2-amino-imidazoyl, tetrahydrofurano, pyrrolo, tetrahydrothiophen-yl, hexylmethyleneimino and heptylmethyleneimino.

[0054] The term "substituted heterocycle" or "substituted heterocyclic ring" means the above-described heterocyclic ring is substituted with, for example, one or more, and preferably one or two, substituents which are the same or different which substituents can be halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_{12} alkyl, C_1 to C_{12} alkoxy, C_1 to C_{12} substituted alkoxy, C_1 to C_{12} acyl,

C_1 to C_{12} acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, substituted amino, protected substituted amino, (disubstituted)amino carboxamide, protected carboxamide, N-(C_1 to C_{12} alkyl)carboxamide, protected N-(C_1 to C_{12} alkyl)carboxamide, N, N-di(C_1 to C_{12} alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_{12} alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino, heterocycle or substituted heterocycle groups.

[0055] One or more of the compounds of the invention, even within a given library, may be present as a salt. The term "salt" encompasses those salts that form with the carboxylate anions and amine nitrogens and include salts formed with the organic and inorganic anions and cations discussed below. Furthermore, the term includes salts that form by standard acid-base reactions with basic groups (such as amino groups) and organic or inorganic acids. Such acids include hydrochloric, sulfuric, phosphoric, acetic, succinic, citric, lactic, maleic, fumaric, palmitic, cholic, pamoic, mucic, D-glutamic, D-camphoric, glutaric, phthalic, tartaric, lauric, stearic, salicyclic, methanesulfonic, benzenesulfonic, sorbic, picric, benzoic, cinnamic, and like acids.

[0056] The term "organic or inorganic cation" refers to counter-ions for the carboxylate anion of a carboxylate salt. The counter-ions are chosen from the alkali and alkaline earth metals, (such as lithium, sodium, potassium, barium, aluminum and calcium); ammonium and mono-, di- and tri-alkyl amines such as trimethylamine, cyclohexylamine; and the organic cations, such as dibenzylammonium, benzylammonium, 2-hydroxyethylammonium, bis(2-hydroxyethyl)ammonium, phenylethylbenzylammonium, dibenzylethylenediammonium, and like cations. See, for example, "Pharmaceutical Salts," Berge et al., J. Pharm. Sci., 66:1-19 (1977). Other cations encompassed by the above term include the protonated form of procaine, quinine and N-methylglucosamine, and the protonated forms of basic amino acids such as glycine, ornithine, histidine, phenylglycine, lysine and arginine. Furthermore, any zwitterionic form of the instant compounds formed by a carboxylic acid and an amino group is referred to by this term. For example, a

cation for a carboxylate anion will exist when R_2 or R_3 is substituted with a (quaternary ammonium)methyl group. A preferred cation for the carboxylate anion is the sodium cation.

[0057] The compounds of the invention can also exist as solvates and hydrates. Thus, these compounds may crystallize with, for example, waters of hydration, or one, a number of, or any fraction thereof of molecules of the mother liquor solvent. The solvates and hydrates of such compounds are included within the scope of this invention.

[0058] One or more compounds of the invention, even when in a library, can be in the biologically active ester form, such as the non-toxic, metabolically-labile ester-form. Such ester forms induce increased blood levels and prolong the efficacy of the corresponding non-esterified forms of the compounds. Ester groups which can be used include the lower alkoxymethyl groups, for example, methoxymethyl, ethoxymethyl, isopropoxymethyl and the like; the -(C_1 to C_7) alkoxyethyl groups, for example methoxyethyl, ethoxyethyl, propoxyethyl, isopropoxyethyl and the like; the 2-oxo-1,3-diooxlen-4-ylmethyl groups, such as 5-methyl-2-oxo-1,3-dioxolen-4-ylmethyl, 5-phenyl-2-oxo-1,3-dioxolen-4-ylmethyl and the like; the C_1 to C_4 alkylthiomethyl groups, for example methylthiomethyl, ethylthiomethyl, iso-propylthiomethyl and the like; the acyloxymethyl groups, for example pivaloyloxymethyl, pivaloyloxyethyl, -acetoxymethyl and the like; the ethoxycarbonyl-1-methyl group; the -acetoxyethyl; the 1-(C_1 to C_7 alkyloxycarbonyloxy)ethyl groups such as the 1-(ethoxycarbonyloxy)ethyl group; and the 1-(C_1 to C_7 alkylaminocarbonyloxy)ethyl groups such as the 1-(methylaminocarbonyloxy)ethyl group.

[0059] The term "amino acid" includes any one of the twenty naturally-occurring amino acids or the D-form of any one of the naturally-occurring amino acids. In addition, the term "amino acid" also includes other non-naturally occurring amino acids besides the D-amino acids, which are functional equivalents of the naturally-occurring amino acids. Such non-naturally-occurring amino acids include, for example, norleucine ("Nle"), norvaline ("Nva"), L- or D-naphthalanine, ornithine ("Orn"), homoarginine (homoArg) and others well known

in the peptide art, such as those described in M. Bodanzsky, "Principles of Peptide Synthesis," 1st and 2nd revised ed., Springer-Verlag, New York, NY, 1984 and 1993, and Stewart and Young, "Solid Phase Peptide Synthesis," 2nd ed., Pierce Chemical Co., Rockford, IL, 1984. Amino acids and amino acid analogs can be purchased commercially (Sigma Chemical Co.; Advanced Chemtech) or synthesized using methods known in the art.

[0060] The term "functionalized resin" means any resin, crosslinked or otherwise, where functional groups have been introduced into the resin, as is common in the art. Such resins include, for example, those functionalized with amino, alkylhalo, formyl or hydroxy groups. Such resins which can serve as solid supports are well known in the art and include, for example, 4-methylbenzhydrylamine-copoly(styrene-1% divinylbenzene) (MBHA), 4-hydroxymethylphenoxymethyl-copoly(styrene-1% divinylbenzene), 4-oxymethyl-phenyl-acetamido-copoly(stryene-1% divinylbenzene)(Wang), 4-(oxymethyl)-phenylacetamido methyl (Pam), and Tentagel™, from Rapp Polymere Gmbh, trialkoxy-diphenyl-methyl ester- copoly(styrene-1% divinylbenzene)(RINK) all of which are commercially available. Other functionalized resins are known in the art and can be use without departure from the scope of the current invention. Such resins may include those described in Jung, G., Combinatorial Peptide and Nonpeptide Libraties, A Handbook (VCH Verlag, 1996) or Bunin, B. A., The Combinatorial Index (Academic Press, 1998).

[0061] As used herein, a "combinatorial library" is an intentionally created collection of differing molecules which can be prepared by the means provided below or otherwise and screened for biological activity in a variety of formats (e.g., libraries of soluble molecules, libraries of compounds attached to resin beads, silica chips or other solid supports). A "combinatorial library," as defined above, involves successive rounds of chemical syntheses based on a common starting structure. The combinatorial libraries can be screened in any variety of assays, such as those detailed below as well as others useful for assessing their biological activity. The combinatorial libraries will generally have at least one active compound and are generally prepared such that the compounds are in

equimolar quantities.

[0062] A combinatorial library of the invention can contain one or more of the above-described compounds. The invention further provides a combinatorial library containing five or more of the above-described compounds. In another embodiment of the invention, a combinatorial library can contain ten or more of the above-described compounds. In yet another embodiment of the invention, a combinatorial library can contain fifty or more of the above-described compounds. If desired, a combinatorial library of the invention can contain 100,000 or more, or even 1,000,000 or more, of the above-described compounds.

[0063] By way of example, the preparation of the combinatorial libraries can use the "split resin approach." The split resin approach is described by, for example, U.S. Patent 5,010,175 to Rutter, WO PCT 91/19735 to Simon, and Gallop et al., *J. Med. Chem.*, 37:1233-1251 (1994).

[0064] For preparing pharmaceutical compositions containing compounds of the invention, inert, pharmaceutically acceptable carriers are used. The pharmaceutical carrier can be either solid or liquid. Solid form preparations include, for example, powders, tablets, dispersible granules, capsules, cachets, and suppositories.

[0065] A solid carrier can be one or more substances which can also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders, or tablet disintegrating agents; it can also be an encapsulating material.

[0066] In powders, the carrier is generally a finely divided solid which is in a mixture with the finely divided active component. In tablets, the active compound is mixed with the carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

[0067] For preparing pharmaceutical composition in the form of suppositories, a low-melting wax such as a mixture of fatty acid glycerides and cocoa butter is first melted and the active ingredient is dispersed therein by, for example, stirring. The molten homogeneous mixture is then poured into convenient-sized molds and allowed to cool and solidify.

[0068] Powders and tablets preferably contain between about 5% to about 70% by weight of the active ingredient. Suitable carriers include, for example, magnesium carbonate, magnesium stearate, talc, lactose, sugar, pectin, dextrin, starch, tragacanth, methyl cellulose, sodium carboxymethyl cellulose, a low-melting wax, cocoa butter and the like.

[0069] The pharmaceutical compositions can include the formulation of the active compound with encapsulating material as a carrier providing a capsule in which the active component (with or without other carriers) is surrounded by a carrier, which is thus in association with it. In a similar manner, cachets are also included. Tablets, powders, cachets, and capsules can be used as solid dosage forms suitable for oral administration.

[0070] Liquid pharmaceutical compositions include, for example, solutions suitable for oral or parenteral administration, or suspensions, and emulsions suitable for oral administration. Sterile water solutions of the active component or sterile solutions of the active component in solvents comprising water, ethanol, or propylene glycol are examples of liquid compositions suitable for parenteral administration.

[0071] Sterile solutions can be prepared by dissolving the active component in the desired solvent system, and then passing the resulting solution through a membrane filter to sterilize it or, alternatively, by dissolving the sterile compound in a previously sterilized solvent under sterile conditions.

[0072] Aqueous solutions for oral administration can be prepared by dissolving the active compound in water and adding suitable flavorants, coloring agents, stabilizers, and thickening agents as desired. Aqueous suspensions for oral use can be made by dispersing the finely divided active component in water together with a viscous material such as natural or synthetic gums, resins, methyl cellulose, sodium carboxymethyl cellulose, and other suspending agents known to the pharmaceutical formulation art.

[0073] Preferably, the pharmaceutical composition is in unit dosage form. In such form, the composition is divided into unit doses containing appropriate quantities of the active piperidine-3-carboxamide. The unit dosage form can be a

packaged preparation, the package containing discrete quantities of the preparation, for example, packeted tablets, capsules, and powders in vials or ampules. The unit dosage form can also be a capsule, cachet, or tablet itself, or it can be the appropriate number of any of these packaged forms.

[0074] As pharmaceutical compositions for treating infections, pain, or any other indication the compounds of the present invention are generally in a pharmaceutical composition so as to be administered to a subject at dosage levels of from 0.7 to 7000 mg per day, and preferably 1 to 500 mg per day, for a normal human adult of approximately 70 kg of body weight, this translates into a dosage of from 0.01 to 100 mg/kg of body weight per day. The specific dosages employed, however, can be varied depending upon the requirements of the patient, the severity of the condition being treated, and the activity of the compound being employed. The determination of optimum dosages for a particular situation is within the skill of the art.

[0075] Variant piperidine-3-carboxamide derivative compounds and combinatorial libraries can be prepared as shown in figures 1 and 2 in order to achieve a high level of diversity.

[0076] Resins suitable for use in the present invention can easily be determined by one skilled in the art. Such resins include but are not limited to polystyrene resin (e.g. Wang resin : *p*-benzyloxybenzyl alcohol-polystyrene) and PEG-grafted polystyrene resin (e.g. Tentagel, Argogel).

[0077] Other suitable resins known in the art can be found in "Solid Phase Synthesis and Combinatorial Technologies", Seneci, P.; John Wiley and Sons, 2000, p 1-45.

[0078] The resulting compound can be cleaved from the resin. Resin-bound piperidine-3-carboxamide derivative compounds can be cleaved by treating them, for example, with HF. They can also be cleaved with TFA/DCM, provided that TFA sensitive protecting group such as Boc are not used in the synthetic scheme. The compounds can be extracted from the spent resin, for example, with AcOH.

[0079] The nonsupport-bound combinatorial libraries can be screened as

single compounds. In addition, the nonsupport-bound combinatorial libraries can be screened as mixtures in solution in assays such as radio-receptor inhibition assays, anti-bacterial assays, anti-fungal assays, calmodulin-dependent phosphodiesterase (CaMPDE) assays and phosphodiesterase (PDE) assays, as described in detail below. Deconvolution of highly active mixtures can then be carried out by iterative or positional scanning methods. These techniques, the iterative approach or the positional scanning approach, can be utilized for finding other active compounds within the combinatorial libraries of the present invention using any one of the below-described assays or others well known in the art.

[0080] The iterative approach is well-known and is set forth in general in Houghten *et al.*, *Nature*, 354, 84-86 (1991) and Dooley *et al., Science*, 266, 2019-2022 (1994), both of which are incorporated herein by reference. In the iterative approach, for example, sub-libraries of a molecule having three variable groups are made wherein the first variable is defined. Each of the compounds with the defined variable group is reacted with all of the other possibilities at the other two variable groups. These sub-libraries are each tested to define the identity of the second variable in the sub-library having the highest activity in the screen of choice. A new sub-library with the first two variable positions defined is reacted again with all the other possibilities at the remaining undefined variable position. As before, the identity of the third variable position in the sub-library having the highest activity is determined. If more variables exist, this process is repeated for all variables, yielding the compound with each variable contributing to the highest desired activity in the screening process. Promising compounds from this process can then be synthesized on larger scale in traditional single-compound synthetic methods for further biological investigation.

[0081] The positional-scanning approach has been described for various combinatorial libraries as described, for example, in R. Houghten *et al.* PCT/US91/08694 and U.S. Patent 5,556,762, both of which are incorporated herein by reference. In the positional scanning approach, sublibraries are made defining only one variable with each set of sublibraries and all possible sublibraries with each single variable defined (and all other possibilities at all of

the other variable positions), made and tested. From the instant description one skilled in the art could synthesize combinatorial libraries wherein two fixed positions are defined at a time. From the testing of each single-variable defined combinatorial library, the optimum substituent at that position can be determined, pointing to the optimum or at least a series of compounds having a maximum of the desired biological activity. Thus, the number of sublibraries for compounds with a single position defined will be the number of different substituents desired at that position, and the number of all the compounds in each sublibrary will be the product of the number of substituents at each of the other variables.

[0082] Individual compounds and pharmaceutical compositions containing the compounds, as well as methods of using the same, are included within the scope of the present invention. The compounds of the present invention can be used for a variety of purposes and indications and as medicaments for any such purposes and indications. For example, piperidine-3-carboxamide derivative compounds of the present invention can be used as pesticides, acaricides, receptor agonists or antagonists and antimicrobial agents, including antibacterial or antiviral agents. The libraries can be screened in any variety of melanocortin receptor and related activity assays, such as those detailed below as well as others known in the art. Additionally, the subject compounds can be useful as analgesics. Assays which can be used to test the biological activity of the instant compounds include antimicrobial assays, a competitive enzyme-linked immunoabsorbent assay and radio-receptor assays, as described below.

[0083] The melanocortin (MC) receptors are a group of cell surface proteins that mediate a variety of physiological effects, including regulation of adrenal gland function such as production of the glucocorticoids cortisol and aldosterone; control of melanocyte growth and pigment production; thermoregulation; immunomodulation; and analgesia. Five distinct MC receptors have been cloned and are expressed in a variety of tissues, including melanocytes, adrenal cortex, brain, gut, placenta, skeletal muscle, lung, spleen, thymus, bone marrow, pituitary, gonads and adipose tissue (Tatro, Neuroimmunomodulation 3:259-284 (1996)). Three MC receptors, MCR-1, MCR-3 and MCR-4, are expressed in

brain tissue (Xia et al., Neuroreport 6:2193-2196 (1995)).

[0084] A variety of ligands termed melanocortins function as agonists that stimulate the activity of MC receptors. The melanocortins include melanocyte-stimulating hormones (MSH) such as α-MSH, β-MSH and γ-MSH, as well as adrenocorticotropic hormone (ACTH). Individual ligands can bind to multiple MC receptors with differing relative affinities. The variety of ligands and MC receptors with differential tissue-specific expression likely provides the molecular basis for the diverse physiological effects of melanocortins and MC receptors. For example, α-MSH antagonizes the actions of immunological substances such as cytokines and acts to modulate fever, inflammation and immune responses (Catania and Lipton, Annals N. Y. Acad. Sci. 680:412-423 (1993)).

[0085] The role of certain specific MC receptors in some of the physiological effects described above for MC receptors has been elucidated. For example, MCR-1 is involved in pain and inflammation. MCR-1 mRNA is expressed in neutrophils (Catania et al., Peptides 17:675-679 (1996)). The anti-inflammatory agent α-MSH was found to inhibit migration of neutrophils. Thus, the presence of MCR-1 in neutrophils correlates with the anti-inflammatory activity of α-MSH.

[0086] An interesting link of MC receptors to regulation of food intake and obesity has recently been described. The brain MC receptor MCR-4 has been shown to function in the regulation of body weight and food intake. Mice in which MCR-4 has been knocked out exhibit weight gain (Huszar et al., Cell 88:131-141 (1997)). In addition, injection into brain of synthetic peptides that mimic melanocortins and bind to MCR-4 caused suppressed feeding in normal and mutant obese mice (Fan et al., Nature 385:165-168 (1997)). These results indicate that the brain MC receptor MCR-4 functions in regulating food intake and body weight.

[0087] Due to the varied physiological activities of MC receptors, high affinity ligands of MC receptors could be used to exploit the varied physiological responses of MC receptors by functioning as potential therapeutic agents or as lead compounds for the development of therapeutic agents. Furthermore, due to

the effect of MC receptors on the activity of various cytokines, high affinity MC receptor ligands could also be used to regulate cytokine activity.

[0088] A variety of assays can be used to identify or characterize MC receptor ligands of the invention. For example, the ability of a piperidine-3-carboxamide derivative compound to compete for binding of a known MC receptor ligand can be used to assess the affinity and specificity of a piperidine-3-carboxamide derivative compound for one or more MC receptors. Any MC receptor ligand can be used so long as the ligand can be labeled with a detectable moiety. The detectable moiety can be, for example, a radiolabel, fluorescent label or chromophore, or any detectable functional moiety so long as the MC receptor ligand exhibits specific MC receptor binding. A particularly useful detectable MC receptor ligand for identifying and characterizing other MC receptor ligands is 125I-HP 467, which has the amino acid sequence Ac-Nle-Gln-His-(*p*(I)-D-Phe)-Arg-(D-Trp)-Gly-NH2 and is described in Dooley et al., "Melanocortin Receptor Ligands and Methods of Using Same," U.S. patent application 09/027,108, filed February 20, 1998, which is incorporated herein by reference. HP 467 is a *para*-iodinated form of HP 228.

[0089] Using assay methods such as those described above, binding kinetics and competition with radiolabeled HP 467 can confirm that piperidine-3-carboxamide derivative compounds of the invention bind to one or more MC receptors. Furthermore, piperidine-3-carboxamide derivative compounds of the invention can exhibit a range of affinities and specificity for various MC receptors.

[0090] The invention provides MC receptor ligands that can bind to several MC receptors with similar affinity. In addition, the invention also provides MC receptor ligands that can be selective for one or more MC receptors. As used herein, the term "selective" means that the affinity of a MC receptor ligand differs between one MC receptor and another by about 10-fold, generally about 20- to 50-fold, and particularly about 100-fold. In some cases, a MC receptor ligand having broad specificity is desired. In other cases, it is desirable to use MC receptor ligands having selectivity for a particular MC receptor. For example, MCR-1 ligands are particularly useful for treating pain and inflammation, whereas

MCR-4 ligands are useful for treating obesity. The binding characteristics and specificity of a given MC receptor ligand can be selected based on the particular disease or physiological effect that is desired to be altered.

[0091] Another assay useful for identifying or characterizing MC receptor ligands measures signaling of MC receptors. MC receptors are G protein-coupled receptors that couple to adenylate cyclase and produce cAMP. Therefore, measuring cAMP production in a cell expressing a MC receptor and treated with a MC receptor ligand can be used to assess the function of the MC receptor ligand in activating a MC receptor.

[0092] Ligands for MC-3 that can alter the activity of an MC-3 receptor can be useful for treating sexual dysfunction and other conditions or conditions associated with MC-3 such as inflammation. Other MC-3-associated conditions that can be treated with the MC-3 receptor ligands include disuse deconditioning; organ damage such as organ transplantation or ischemic injury; adverse reactions associated with cancer chemotherapy; diseases such as atherosclerosis that are mediated by free radicals and nitric oxide action; bacterial endotoxic sepsis and related shock; adult respiratory distress syndrome; and autoimmune or other patho-immunogenic diseases or reactions such as allergic reactions or anaphylaxis, rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, glomerulonephritis, systemic lupus erythematosus, transplant atherosclerosis and parasitic mediated immune dysfunctions such as Chagas's disease.

[0093] The invention further provides a method for treating an MC-3-associated condition in a subject. The term "MC-3-associated condition" includes any condition or condition mediated by MC-3 or can be affected by binding an MC-3 ligand. Such conditions include inflammation and sexual dysfunction.

[0094] The term "sexual dysfunction" herein means any condition that inhibits or impairs normal sexual function, including coitus. However, the term need not be limited to physiological conditions, but may include psychogenic conditions or perceived impairment without a formal diagnosis of pathology.

[0095] In males, sexual dysfunction includes erectile dysfunction. The term "erectile dysfunction" or "impotence" means herein the inability or impaired ability to attain or sustain an erection that would be of satisfactory rigidity for coitus. Sexual dysfunction in males can also include premature ejaculation and priapism, which is a condition of prolonged and sometimes painful erection unrelated to sexual activity, often associated with sickle-cell disease.

[0096] In females, sexual dysfunction includes sexual arousal disorder. The term "sexual arousal disorder" means herein a persistent or recurrent failure to attain or maintain the lubrication-swelling response of sexual excitement until completion of sexual activity. Sexual dysfunction in females can also include inhibited orgasm and dyspareunia, which is painful or difficult coitus. Sexual dysfunction can also be manifested as inhibited sexual desire or inhibited lordosis behavior in animals.

[0097] In addition, the ability of the compounds to inhibit bacterial growth, and therefore be useful to that infection, can be determined by methods well known in the art. Compounds of the present invention can be shown to have antimicrobial activity by the *in vitro* antimicrobial activity assay described below and, therefore, are useful as antimicrobial agents.

[0098] Moreover, an exemplary *in vitro* antimicrobial activity assay is described in Blondelle and Houghten, *Biochemistry* 30:4671-4678 (1991), which is incorporated herein by reference. In brief, *Staphylococcus aureus* ATCC 29213 (Rockville, MD) is grown overnight at 37°C in Mueller-Hinton broth, then re-inoculated and incubated at 37°C to reach the exponential phase of bacterial growth (i.e., a final bacterial suspension containing 105 to 5 x 105 colony-forming units/ml). The concentration of cells is established by plating 100 μl of the culture solution using serial dilutions (e.g., 10-2, 10-3 and 10-4) onto solid agar plates. In 96-well tissue culture plates, compounds, individual or in mixtures, are added to the bacterial suspension at concentrations derived from serial two-fold dilutions ranging from 1500 to 2.9 µg/ml. The plates are incubated overnight at 37°C and the growth determined at each concentration by OD620 nm. The IC50

(the concentration necessary to inhibit 50% of the growth of the bacteria) can then be calculated.

[0099] The competitive ELISA method which can be used here is a modification of the direct ELISA technique described previously in Appel et al., J. Immunol. 144:976-983 (1990), which is incorporated herein by reference. It differs only in the MAb addition step. Briefly, multi-well microplates are coated with the antigenic peptide (Ac-GASPYPNLSNQQT-NH2) at a concentration of 100 pmol/50 µl. After blocking, 25 µl of a 1.0 mg/ml solution of each mixture of a synthetic combinatorial library (or individual compound) is added, followed by MAb 125-10F3 (Appel et al., *supra*) (25 µl per well). The MAb is added at a fixed dilution in which the bicyclic guanidine in solution effectively competes for MAb binding with the antigenic peptide adsorbed to the plate. The remaining steps are the same as for direct ELISA. The concentration of compound necessary to inhibit 50% of the MAb binding to the control peptide on the plate (IC50) is determined by serial dilutions of the compound.

[0100] Alternative screening can be done with radio-receptor assays. The radio-receptor assay, can be selective for any one of the µ, κ, or δ opiate receptors. Compounds of the present invention can be useful in vitro for the diagnosis of relevant opioid receptor subtypes, such as κ, in the brain and other tissue samples. Similarly, the compounds can be used *in vivo* diagnostically to localize opioid receptor subtypes.

[0101] The radio-receptor assays are also an indication of the compounds' analgesic properties as described, for example, in Dooley et al., *Proc. Natl. Acad. Sci.*, 90:10811-10815 (1993). For example, it can be envisioned that these compounds can be used for therapeutic purposes to block the peripheral effects of a centrally acting pain killer. For instance, morphine is a centrally acting pain killer. Morphine, however, has a number of deleterious effects in the periphery which are not required for the desired analgesic effects, such as constipation and pruritus (itching). While it is known that the many compounds do not readily cross the blood-brain barrier and, therefore, elicit no central effect, the subject

compounds can have value in blocking the periphery effects of morphine, such as constipation and pruritus. Accordingly, the subject compounds can also be useful as drugs, namely as analgesics, or to treat pathologies associated with other compounds which interact with the opioid receptor system.

[0102] Additionally, such compounds can be tested in a σ receptor assay. Ligands for the σ receptor can be useful as antipsychotic agents, as described in Abou-Gharbia et al., *Annual Reports in Medicinal Chemistry*, 28:1-10 (1993).

[0103] Radio-receptor assays can be performed with particulate membranes prepared using a modification of the method described in Pasternak et al., *Mol. Pharmacol.* 11:340-351 (1975), which is incorporated herein by reference. Rat brains frozen in liquid nitrogen can be obtained from Rockland (Gilbertsville, PA). The brains are thawed, the cerebella removed and the remaining tissue weighed. Each brain is individually homogenized in 40 ml Tris-HCl buffer (50 mM, pH 7.4, 4°C) and centrifuged (Sorvall® RC5C SA-600: Du Pont, Wilmington, DE) (16,000 rpm) for 10 minutes. The pellets are resuspended in fresh Tris-HCl buffer and incubated at 37°C for 40 minutes. Following incubation, the suspensions are centrifuged as before, the resulting pellets resuspended in 100 volumes of Tris buffer and the suspensions combined. Membrane suspensions are prepared and used in the same day. Protein content of the crude homogenates generally range from 0.15-0.2 mg/ml as determined using the method described in Bradford, M.M., *Anal. Biochem.* 72:248-254 (1976), which is incorporated herein by reference.

[0104] Binding assays are carried out in polypropylene tubes, each tube containing 0.5 ml of membrane suspension. 8 nM of 3H-[D-Ala2,Me-Phe4,Gly-ol5]enkephalin (DAMGO) (specific activity = 36 Ci/mmol, 160,000 cpm per tube; which can be obtained from Multiple Peptide Systems, San Diego, CA, through NIDA drug distribution program 271-90-7302) and 80 µg/ml of bicyclic guanidine, individual or as a mixture and Tris-HCl buffer in a total volume of 0.65 ml. Assay tubes are incubated for 60 mins. at 25°C. The reaction is terminated by filtration through GF-B filters on a Tomtec harvester (Orange, CT). The filters are

subsequently washed with 6 ml of Tris-HCl buffer, 4°C. Bound radioactivity is counted on a Pharmacia Biotech Betaplate Liquid Scintillation Counter (Piscataway, NJ) and expressed in cpm. To determine inter- and intra-assay variation, standard curves in which 3H-DAMGO is incubated in the presence of a range of concentrations of unlabeled DAMGO (0.13-3900 nM) are generally included in each plate of each assay (a 96-well format). Competitive inhibition assays are performed as above using serial dilutions of the piperidine-3-carboxamides, individually or in mixtures. IC50 values (the concentration necessary to inhibit 50% of 3H-DAMGO binding) are then calculated. IC50 values of less than 1000 nM are indicative of highly active opioid compounds which bind to the μ receptor, with particularly active compounds having IC50 values of 100 nM or less and the most active compounds with values of less than 10 nM.

[0105] As opposed to this μ receptor selective assay, which can be carried out using 3H-DAMGO as radioligand, as described above, assays selective for κ receptors can be carried out using [3H]-U69,593 (3 nM, specific activity 62 Ci/mmol) as radioligand. Assays selective for δ opiate receptors can be carried out using tritiated DSLET ([D-Ser2, D-Leu5]-threonine-enkephalin) as radioligand. Assays selective for the σ opiate receptor can use radiolabeled pentazocine as ligand.

[0106] Screening of combinatorial libraries and compounds of the invention can be done with an anti-fungal assay. Compounds of the present invention can be useful for treating fungal infections.

[0107] Screening of combinatorial libraries and compounds of the invention also can be done with a calmodulin-dependent phosphodiesterase (CaMPDE) assay. Compounds of the present invention can be useful as calmodulin antagonists.

[0108] Calmodulin (CaM), which is the major intracellular calcium receptor, is involved in many processes that are crucial to cellular viability. In particular, calmodulin is implicated in calcium-stimulated cell proliferation. Calmodulin

antagonists are, therefore, useful for treating conditions associated with increased cell proliferation, for example, cancer. In addition, calmodulin antagonists such as compounds of the subject invention are useful both in vitro and in vivo for identifying the role of calmodulin in other biological processes. The disadvantages of known antagonists such as trifluoperazine and N-(4-aminobutyl)-5-chloro-2-naphthalenesulfonamide (W13) include their non-specificity and toxicity. In contrast, advantages of the combinatorial libraries and compounds of the subject invention as calmodulin antagonists include their reduced flexibility and ability to generate broader conformational space of interactive residues as compared to their linear counterparts.

[0109] An example of an assay that identifies CaM antagonists is a CaMPDE assay. In brief, samples are mixed with 50 µl of assay buffer (360 mM Tris, 360 mM Imidazole, 45 mM Mg(CH3COO)2, pH 7.5) and 10 µl of CaCl2 (4.5 mM) to a final volume of 251 µl. 25 µl of calmodulin stock solution (Boehringer Mannheim; 0.01 µg/µl) is then added and the samples then sit at room temperature for 10 minutes. 14 µl of PDE (Sigma; 2 Units dissolved in 4 ml of water; stock concentration: 0.0005 Units/µl) is then added, followed by 50 µl of 5'-nucleotidase (Sigma; 100 Units dissolved in 10 ml of 10 mM Tris-HCl containing 0.5 mM Mg(CH3COO)2, pH 7.0; stock concentration: 10 Units/ml). The samples are then incubated for 10 minutes at 30°C. 50 μl of adenosine 3',5'-cyclic monophosphate (cAMP) (20 mM in water at pH 7.0) is added, the samples incubated for 1 hour at 30°C and then vortexed. 200 μl of trichloroacetic acid (TCA) (55% in water) is added to a 200 μl sample aliquot, which is then vortexed and centrifuged for 10 minutes. 80 µl of the resulting supernatants of each sample is transferred to a 96-well plate, with 2 wells each containing 80 µl of each sample. 80 µl of ammonium molybdate (1.1% in 1.1N H2SO4) is then added to all the wells, and the OD of each were determined at 730nm, with the values later subtracted to the final OD reading. 16 µl of reducing agent (6g sodium bisulfite, 0.6g sodium sulfite and 125mg of 1-amino-2-naphtol-4-sulfonic acid in 50ml of water) is then added to one of each sample duplicate and 16 µl of water is added to the other duplicate. After sitting for 1 hour at room

temperature, the OD of each well is determined at 730nm. The percent inhibition of calmodulin activity is then calculated for each sample, using as 0% inhibition a control sample containing all reagents without any test samples and as 100% inhibition a control sample containing test samples and all reagents except calmodulin. In addition, the percent inhibition of phosphodiesterase activity was determined by following a similar protocol as the CaMPDE assay described above, except not adding calmodulin to the sample mixture and calculating the percent inhibition by using as 0% inhibition a control reagent without any test samples and as 100% inhibition a control sample containing test samples and all reagents except cAMP.

[0110] The following examples are provided to illustrate but not limit the present invention. The following abreviations have the corresponding meanings:

DMF : N,N-dimethylforamide;
HOBt : 1-hydroxybenzotriazole;
Boc : tert-butoxycarbonyl;
DIC : N,N=-diisopropylcarbodiimide;
TFA : trifluoroacetic acid;
DIEA : N,N-diisopropylethylamine;
DCM : dichloromethane;
RT : room temperature
MeOH: methanol
MeOEtOH : 2-methoxyethanol
DCE : 1,2-dichloroethane
THF : tetrahydrofuran
ACN : acetonitrile
Wang resin : *p*-benzyloxybenzyl alcohol-polystyrene Br-Wang resin : *p*-benzyloxybenzyl bromide-polystyrene
PP : polypropylene
PPh3Br2 : triphenylphosphine dibromide
DMAP : 4-dimethylamino-pyridine

Example 1

Synthetic Protocol

Step 1a. Loading Hydroxybenzaldehydes on Bromo-Wang Resin

[0111] A 1 L Pyrex media bottle was charged with 100 g Bromo-Wang resin (100-200 mesh, 1.4 mmol/g). DMF (350 ml) was added and the bottle was shaken by hand to distribute the solvent within the swollen resin. A 500 ml Pyrex media bottle was charged with the hydroxybenzaldehyde (420 mmol, 3 eq) and the aldehyde was dissolved in DMF (300 ml). The aldehyde solution was cooled to 0° C (ice bath) and potassium *tert*-butoxide (44.8 g, 400 mmol) was added in two equal portions shaking for about 5 min. between additions. CAUTION: EXOTHERMIC REACTION. The temperature must be maintained at or below 25° C. The bottle was removed from the ice bath and shaken periodically to help dissolve the potassium *tert*-butoxide completely. After the second portion of potassium *tert*-butoxide was added, the bottle was allowed to warm to 25° C. After 30 min. at 25° C, all the potassium *tert*-butoxide dissolved and the solutions had various dark colors. The phenoxide solution was added to the swollen resin in two portions, shaking between portions. The 1L bottles were clamped horizontally in an orbital shaker oven and allowed to shake at 25° C for 30 min. The temperature was then increased to 50° C and the reaction allowed to shake for 14 h. After cooling, each resin slurry was poured into a 8" x 10" 3-sided porous polypropylene packet (tea bag) sitting in a 2 L beaker. After the solvent mixture had drained from the resin, the fourth side of the tea bag was sealed and the tea bags were washed in wide-mouth HDPE Nalgene bottles as follows: 2 x DMF, 4 x DMF/H_2O (4:1), 3 x DMF, 4 x MeOH. The tea bags were allowed to air dry in a fume hood.

Step 1b. Loading Diamines on Wang-Imidazolide Resin

[0112] For each R_1 diamine, a 4 L Nalgene bottle was charged with 17 x 2.5 g

tea bags containing Wang resin (100-200 mesh, 1.4 mmol/g). DCM (2 L) was added followed by 1,1'-carbonyldiimidazole (97 g, 0.60 mol, 0.3 M). The bags were shaken for 3 h at room temperature. Each diamine (0.72 mol, 0.4 M) was placed in a 2 L Nalgene bottle and 1.8 L of DCM added.

[0113] After 3 h shaking with CDI, the Wang-imidazolide tea bags were washed quickly with DCM (x2). The diamine solution was added immediately and the bags shaken overnight at room temperature. The bags were washed with DCM (x3) and MeOH (x3).

Step 2a. Imine Formation for the R_1 Hydroxybenzaldehydes.

[0114] After splitting the tea bags from step 1a, each set of 8 x 2.5 g bags was placed into a 1 L Nalgene bottle. The containers were then filled with 250 ml of trimethylorthoformate and 250 ml of anhydrous DMF. After the bags were saturated with the solvent, the primary amine (150 mmol, 0.3 M) was added. The reaction was then allowed to shake at room temperature for 24 h. The wash procedure must be carried out just before step 3 and the description is included in that section.

Step 2b. Imine Formation for the R_1 Primary Diamines.

[0115] After splitting the tea bags from step 1b, each set of 7 x 2.5 g bags was placed into a 1 L Nalgene bottle. The containers were then filled with 250 ml of trimethylorthoformate and 250 ml of anhydrous DMF. After the bags were saturated with the solvent, the aldehyde (150 mmol, 0.3 M) was added. The reaction was then shaken at room temperature for 24 h. The wash procedure must be carried out just before step 3 and is described in that section.

Step 3. Cyclization with 2-Phenylglutaric Anhydride

[0116] In an 8L Nalgene bottle, 2-Phenylglutaric anhydride (1.0 mol, 0.4M) was completely dissolved in 2.5L anhydrous DMF and triethylamine (0.03 M) was added. This anhydride solution is created before washing the imine tea bags. The imine tea bags from step 2 (60 X 2.5g bags) were quickly washed with

anhydrous DMF (3 x, 3 minutes or less washing). After washing, the imine bags were immediately transferred to the 2-Phenylglutaric anhydride solution and the reaction shaken at RT for 5 days. The bags were washed with DMF (x3) DCM (x3) and MeOH (x3) and air-dried.

Step 4. Acylation of the Resin Bound Carboxylic Acid.

[0117] Each tea bag from step 3 was plated into 40 wells of a 2 ml deep-well microtiter plate. The resin bound carboxylic acid was pre-activated by treatment with 0.6 ml of a solution containing 0.6 M DIC, 0.6M HOBt in anhydrous DMF. The plates were allowed to stand for one hour at room temperature. During this time, each amine solution was prepared by dissolving the amine (0.6M) in a solution of DIEA (0.8 M) in DMF. To each well containing the pre-activated acid resin was added 0.6 ml of the amine solution. The final concentrations in each well were: amine (0.3M), DIEA (0.4 M), HOBt (0.3 M), and DIC (0.3 M). The plates were vortexed and were placed in a shaker oven at 50° C for 24 h. After cooling to room temperature, the resin was washed using a robotic wash station with 20% water/DMF (x2), DMF (x8) and MeOH (x6) and air-dried.

Step 5. Cleavage from Linker and Extraction

[0118] To dry microtiter plates was added 0.5 ml of 20% TFA/DCM to each well. The plates were capped and placed on a shaker at room temperature for 2 h. The plates were transferred to a GENEVAC to remove the volatile TFA/DCM solution. The resin was extracted with AcOH and the extracts were frozen and lyophilized to afford the products as yellow oils. All of the final products were analyzed by HPLC/MS using ELSD detection to determine purity.

Example 2

Preparation of (Substituted Phenyl)-glutaric anhydrides

[0119] The appropriate substituted phenylacetic acid ethyl or methyl ester **1** (0.01 mol) is dissolved in anhydrous ethanol (100 ml). To this solution is added

Sodium ethoxide (0.01 mol), followed by ethyl acrylate (0.015 mol), and the solution is heated to reflux overnight. The solution is cooled and the solvent evaporated under reduced pressure. The product **2** is then dissolved in 100 ml H2O/EtOH 1:1 and KOH added (0.10 mol). The solution is heated to reflux for 10 hours, acidified to pH 3 with 1 N HCl and the diacid product **3** extracted with EtOAc, washed with water and brine, and dried with MgSO4. After removal of the solvent, the resulting solid is suspended in Acetic anhydride (100 ml) and heated to reflux for 1 hour to afford the anhydride. The solvent is removed and the residue is suspended in toluene and evaporated to afford the product **4**.

List of Compounds **1**:
ETHYL 2-THIOPHENEACETATE
ETHYL THIOPHENE-3-ACETATE
INDOLE-3-ACETIC ACID ETHYL ESTER
ETHYL 2-PYRIDYLACETATE
ETHYL 3-PYRIDYLACETATE
ETHYL O-TOLYLACETATE
ETHYL P-TOLYLACETATE
METHYL 1-METHYL-2-PYRROLEACETATE
METHYL 2,3,4,5,6-PENTAFLUOROPHENYLACETATE
ETHYL 2-NAPHTHYLACETATE
METHYL 2-(4,5-DIMETHOXY-2-NITROPHENYL)ACETATE
ETHYL P-BROMOPHENYLACETATE
ETHYL 4-NITROPHENYLACETATE
METHYL 2,3,4-TRIMETHOXYPHENYL ACETATE
METHYL 3,4,5-TRIMETHOXYPHENYL ACETATE
ETHYL 3,4-DIMETHOXYPHENYLACETATE
ETHYL M-TOLYLACETATE
2,4-DICHLOROPHENYLACETIC ACID METHYL ESTER
ETHYL 4-CHLOROPHENYLACETATE
ETHYL 1-NAPHTHYLACETATE
ETHYL 3-METHOXYPHENYLACETATE
ETHYL 4-BENZYLOXYPHENYLACETATE
ETHYL 4-METHOXYPHENYLACETATE
5-BENZYLOXYINDOLE-3-ACETIC ACID METHYL ESTER
ETHYL PYRIDINE-4-ACETATE
METHYL 4-TERT-BUTYLPHENYLACETATE
ETHYL MESITYLACETATE
ETHYL 4-ETHOXYPHENYLACETATE
ETHYL 2-BROMOPHENYLACETATE
4-BUTOXYPHENYLACETIC ACID METHYL ESTER

ETHYL 3,5-DIMETHYLPHENYLACETATE
METHYL 3,5-DIMETHOXYPHENYLACETATE
ETHYL 2-NITROPHENYLACETATE
2-CHLOROPHENYLACETIC ACID METHYL ESTER
METHYL 4-BENZYLOXYPHENYLACETATE
METHYL 5-CHLOROBENZO[B]THIEN-3-YLACETATE
2,6-DICHLOROPHENYLACETIC ACID METHYL ESTER
ETHYL 2,5-DIMETHOXYPHENYLACETATE
METHYL (5-METHYL-2-PHENYLOXAZOL-4-YL)ACETATE
METHYL 5,6-DICHLORO-3-INDOLEACETATE
METHYL 2-(5-METHOXY-2-METHYL-1H-INDOL-3-YL)ACETATE
METHYL (5-METHYL-2-PHENYLTHIAZOL-4-YL)ACETATE
IMIDAZO(2,1-B)THIAZOL-6-YL-ACETIC ACID ETHYL ESTER
(4-CHLORO-2-NITRO-PHENYL)-ACETIC ACID ETHYL ESTER
ETHYL 2-(TRIFLUOROMETHYL)PHENYL ACETATE
ETHYL 2-[2-(ACETYLAMINO)-1,3-THIAZOL-4-YL]ACETATE
(1H-IMIDAZOL-4-YL)-ACETIC ACID METHYL ESTER
(4,5-DIMETHOXY-2-NITRO-PHENYL)-ACETIC ACID ETHYL ESTER
ETHYLFURYL ACETATE
METHYL 2-FLUOROPHENYLACETATE
METHYL 2-CHLORO-6-FLUOROPHENYLACETATE
METHYL 4-FLUOROPHENYLACETATE
METHYL 2-CHLORO-4-FLUOROPHENYL ACETATE
METHYL 3-CHLOROPHENYLACETATE
METHYL 3,4-DICHLOROPHENYLACETATE
ETHYL 2-(2-PHENYL-1,3-THIAZOL-4-YL)ACETATE
ETHYL 3,4-DICHLOROPHENYLACETATE
ETHYL 2-(2-METHYL-1,3-THIAZOL-4-YL)ACETATE
ETHYL 2-[2-[4-(TERT-BUTYL)PHENYL]-1,3-THIAZOL-4-YL]ACETATE
ETHYL 2-[2-(4-CHLOROPHENYL)-1,3-THIAZOL-4-YL]ACETATE
METHYL (2-CYANOPHENYL)ACETATE
METHYL (4-CYANOPHENYL)ACETATE

Example 3

Anti-microbial Screen

[0120] Streptococcus pyogenes (ATCC# 97-03 14289) was grown in Todd Hewitt Broth (THB) (Difco Laboratories #0492-17-6) overnight until reaching an optical density of (OD = 0.636@ 570 nm) by reading 0.1 ml in a 96 well microtiter plate in a Molecular Devices Thermomax. This preparation was kept frozen as stocks in 30% v/v glycerol in 1.5 ml aliquots at -70mC until use. Prior to experiments, 6 ml aliquots were thawed and diluted into 50 ml 2X THB. 60 ul

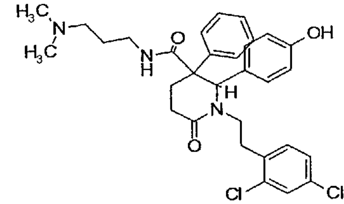
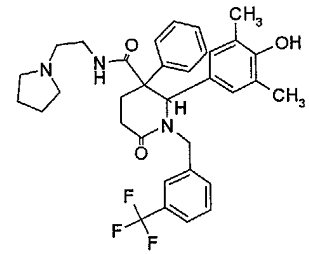
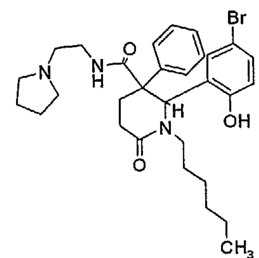
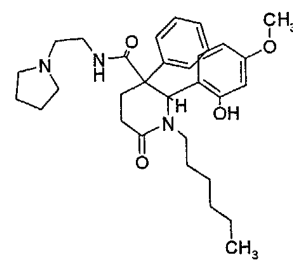
of this dilution was added to 92 wells of microtiter plate. To three wells THB (200 ul) was added to serve as a blank and a sterility control. Test compounds in DMSO and appropriate concentrations of DMSO were added to Growth/Solvent Controls at 0 time. Plates were read at 0 time at 570 nm in the Molecular Devices plate reader to obtain compounds correction factors for insoluble or colored compounds. Plates were read again at 4 hours.

[0121] Percent inhibition is calculated with the following formula

[0122] Color correct = O.D. 0 hr - Blank 0 hr)-(Solvent Control 0hr - Blank 0 hr)

[0123] % Inhibition =

100 - O.D. test compound 4 hr - Blank 4 hr - color correct O.D. growth/solvent control 4 hr - Blank 4 hr

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2979	1	000728122	9100-042	C 04	0.098	99.97	Spy4H	0.1776	TR0910002979	#NAME? 	$C_{31}H_{35}Cl_2N_3O_3$	568.542
9100	682	1	000726065	9100-009	B 07	0.112	98.90	Spy4H	0.1776	TR0910000682	#NAME? 	$C_{34}H_{38}F_3N_3O_3$	593.686
9100	2442	1	000727585	9100-035	B 07	0.17	97.52	Spy4H	0.1776	TR0910002442	#NAME? 	$C_{30}H_{40}BrN_3O_3$	570.568
9100	3002	1	000728145	9100-042	B 07	0.112	97.51	Spy4H	0.1776	TR0910003002	#NAME? 	$C_{31}H_{43}N_3O_4$	521.698

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2989	1	000728132	9100-042	E 05	0.203	97.24	Spy4H	0.1776	TR0910002989	#NAME?	$C_{32}H_{35}Cl_2N_3O_3$	580.552
9100	2482	1	000727625	9100-036	B 02	0.13	96.59	Spy4H	0.1776	TR0910002482	#NAME?	$C_{34}H_{39}Cl_2N_3O_3$	608.606
9100	2509	1	000727652	9100-036	E 05	0.162	96.33	Spy4H	0.1776	TR0910002509	#NAME?	$C_{34}H_{39}Cl_2N_3O_3$	608.606
9100	669	1	000726052	9100-009	E 05	0.207	96.21	Spy4H	0.1776	TR0910000669	#NAME?	$C_{32}H_{35}Cl_2N_3O_3$	580.552

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2722	1	000727865	9100-039	B 02	0.112	95.57	Spy4H	0.1776	TR0910002722	#NAME?	$C_{32}H_{36}ClN_3O_4$	562.106
9100	2449	1	000727592	9100-035	A 08	0.216	95.27	Spy4H	0.1776	TR0910002449	#NAME?	$C_{29}H_{38}BrN_3O_3$	556.541
9100	2467	1	000727610	9100-035	C 10	0.234	94.31	Spy4H	0.1776	TR0910002467	#NAME?	$C_{27}H_{35}BrN_2O_4$	531.487

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3739	1	000728882	9100-051	C 09	0.132	94.27	Spy4H	0.1776	TR0910003739	#NAME?	$C_{34}H_{42}N_4O_4$	570.73
9100	1029	1	000726412	9100-013	E 10	0.162	94.11	Spy4H	0.1776	TR0910001029	#NAME?	$C_{30}H_{41}N_3O_3$	491.672
9100	2402	1	000727545	9100-035	B 02	0.12	92.38	Spy4H	0.1776	TR0910002402	#NAME?	$C_{33}H_{39}N_3O_3$	525.689

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2469	1	000727612	9100-035	E 10	0.231	90.14	Spy4H	0.1776	TR0910002469	#NAME?	$C_{30}H_{40}BrN_3O_3$	570.568
9100	649	1	000726032	9100-009	A 03	0.217	84.40	Spy4H	0.1776	TR0910000649	#NAME?	$C_{31}H_{33}Cl_2N_3O_3$	566.526
9100	2420	1	000727563	9100-035	D 04	0.219	84.37	Spy4H	0.1776	TR0910002420	#NAME?	$C_{33}H_{39}N_3O_3$	525.689

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2474	1	000727617	9100-035	B 11	0.265	84.05	Spy4H	0.1776	TR0910002474	#NAME?	$C_{27}H_{32}BrN_3O_3$	526.472
9100	709	1	000726092	9100-009	E 10	0.178	83.73	Spy4H	0.1776	TR0910000709	#NAME?	$C_{34}H_{38}F_3N_3O_3$	593.686
9100	657	1	000726040	9100-009	A 04	0.188	83.39	Spy4H	0.1776	TR0910000657	#NAME?	$C_{28}H_{28}Cl_2N_2O_4$	527.445

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2602	1	000727745	9100-037	B 07	0.157	83.27	Spy4H	0.1776	TR0910002602	#NAME?	$C_{33}H_{38}ClN_3O_3$	560.134
9100	853	1	000726236	9100-011	E 08	0.28	83.27	Spy4H	0.1776	TR0910000853	#NAME?	$C_{32}H_{28}ClFN_2O_3$	543.035
9100	862	1	000726245	9100-011	F 09	0.255	83.27	Spy4H	0.1776	TR0910000862	#NAME?	$C_{30}H_{33}ClN_2O_4$	521.054
9100	2444	1	000727587	9100-035	D 07	0.275	82.77	Spy4H	0.1776	TR0910002444	#NAME?	$C_{29}H_{35}BrN_4O_3$	567.524

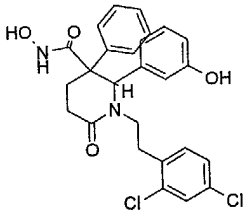
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	995	1	000726378	9100-013	C 06	0.291	82.45	Spy4H	0.1776	TR0910000995	#NAME?	$C_{31}H_{38}BrN_3O_4$	596.562
9100	1699	1	000726842	9100-023	C 04	0.177	82.26	Spy4H	0.1776	TR0910001699	#NAME?	$C_{27}H_{36}BrN_3O_3$	530.503
9100	2997	1	000728140	9100-042	E 06	0.488	82.26	Spy4H	0.1776	TR0910002997	#NAME?	$C_{26}H_{24}Cl_2N_2O_4$	499.392
9100	668	1	000726051	9100-009	D 05	0.328	82.04	Spy4H	0.1776	TR0910000668	#NAME?	$C_{30}H_{32}Cl_2N_2O_4$	555.499

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2419	1	000727562	9100-035	C 04	0.157	81.80	Spy4H	0.1776	TR0910002419	#NAME?	$C_{32}H_{39}N_3O_3$	513.678
9100	868	1	000726251	9100-011	D 10	0.248	81.37	Spy4H	0.1776	TR0910000868	#NAME?	$C_{29}H_{31}ClN_2O_4$	507.027
9100	2441	1	000727584	9100-035	A 07	0.199	79.88	Spy4H	0.1776	TR0910002441	#NAME?	$C_{30}H_{38}BrN_3O_4$	584.551
9100	644	1	000726027	9100-009	D 02	0.211	78.67	Spy4H	0.1776	TR0910000644	#NAME?	$C_{31}H_{30}Cl_2N_4O_3$	577.509

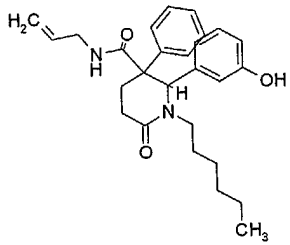
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	846	1	000726229	9100-011	F 07	0.31	78.13	Spy4H	0.1776	TR0910000846	#NAME?	$C_{28}H_{27}ClN_2O_3$	474.985
9100	674	1	000726057	9100-009	B 06	0.275	77.32	Spy4H	0.1776	TR0910000674	#NAME?	$C_{29}H_{27}Cl_2N_3O_3$	536.456
9100	1682	1	000726825	9100-023	B 02	0.193	77.18	Spy4H	0.1776	TR0910001682	#NAME?	$C_{28}H_{36}BrN_3O_3$	542.514

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	870	1	000726253	9100-011	F 10	0.278	76.50	Spy4H	0.1776	TR0910000870	#NAME?	$C_{28}H_{25}ClN_2O_3$	472.97
9100	2476	1	000727619	9100-035	D 11	0.35	75.71	Spy4H	0.1776	TR0910002476	#NAME?	$C_{31}H_{35}BrN_2O_4$	579.531
9100	869	1	000726252	9100-011	E 10	0.255	75.69	Spy4H	0.1776	TR0910000869	#NAME?	$C_{31}H_{34}ClN_3O_3$	532.081

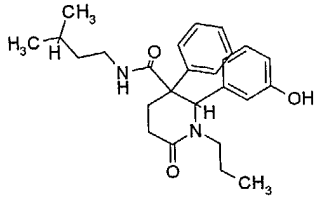
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	677	1	000726060	9100-009	E 06	0.23	75.63	Spy4H	0.1776	TR0910000677	#NAME?	$C_{26}H_{24}Cl_2N_2O_4$	499.392



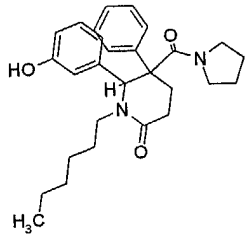
9100	1006	1	000726389	9100-013	F 07	0.334	75.14	Spy4H	0.1776	TR0910001006	#NAME?	$C_{27}H_{34}N_2O_3$	434.577



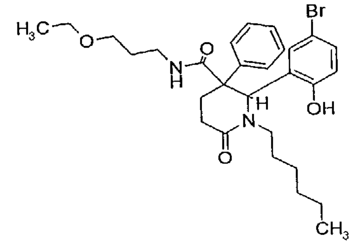
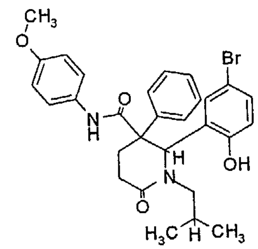
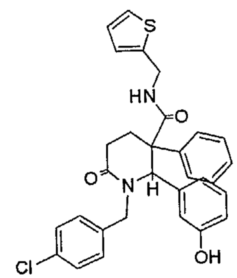
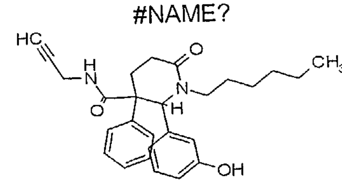
9100	1101	1	000726484	9100-014	E 09	0.263	74.29	Spy4H	0.1776	TR0910001101	#NAME?	$C_{26}H_{34}N_2O_3$	422.566



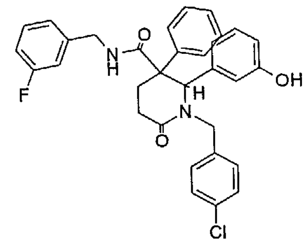
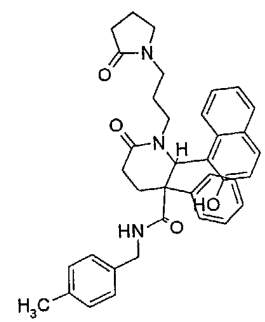
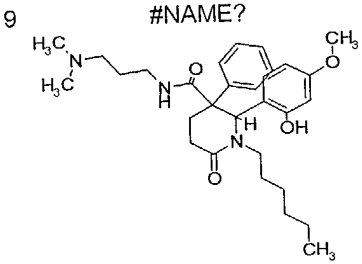
9100	1003	1	000726386	9100-013	C 07	0.302	74.05	Spy4H	0.1776	TR0910001003	#NAME?	$C_{28}H_{36}N_2O_3$	448.603

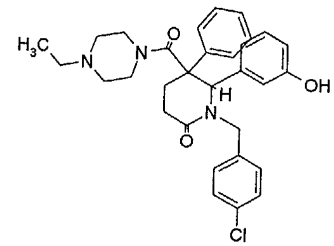
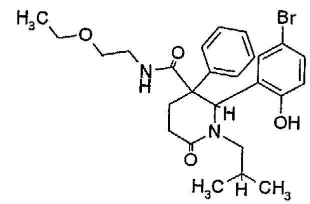
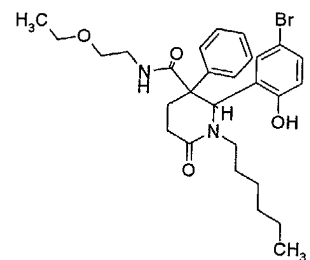
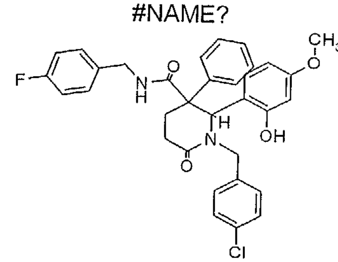


Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	859	1	000726242	9100-011	C 09	0.204	73.80	Spy4H	0.1776	TR0910000859	#NAME?	$C_{30}H_{34}ClN_3O_3$	520.07
9100	2409	1	000727552	9100-035	A 03	0.211	73.79	Spy4H	0.1776	TR0910002409	#NAME?	$C_{32}H_{37}N_3O_3$	511.662
9100	2450	1	000727593	9100-035	B 08	0.294	73.79	Spy4H	0.1776	TR0910002450	#NAME?	$C_{29}H_{37}BrN_2O_4$	557.525

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID				
9100	2462	1	000727605	9100-035	F 09	0.254	73.79	Spy4H	0.1776	TR0910002462		#NAME?	$C_{29} H_{39} Br N_2 O_4$	559.541
9100	1716	1	000726859	9100-023	D 06	0.445	73.16	Spy4H	0.1776	TR0910001716		#NAME?	$C_{29} H_{31} Br N_2 O_4$	551.478
9100	858	1	000726241	9100-011	B 09	0 303	72.99	Spy4H	0 1776	TR0910000858		#NAME?	$C_{30} H_{27} Cl N_2 O_3 S$	531.073
9100	1030	1	000726413	9100-013	F 10	0.28	72.97	Spy4H	0.1776	TR0910001030		#NAME?	$C_{27} H_{32} N_2 O_3$	432.561

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1037	1	000726420	9100-013	E 11	0.26	72.97	Spy4H	0.1776	TR0910001037	#NAME?	$C_{24}H_{30}N_2O_4$	410.511
9100	1075	1	000726458	9100-014	C 06	0.3	72.88	Spy4H	0.1776	TR0910001075	#NAME?	$C_{29}H_{36}N_2O_3$	460.614
9100	867	1	000726250	9100-011	C 10	0.233	72.72	Spy4H	0.1776	TR0910000867	#NAME?	$C_{28}H_{29}ClN_2O_4$	493
9100	2340	1	000727483	9100-033	D 04	0.216	72.56	Spy4H	0.1776	TR0910002340	#NAME?	$C_{32}H_{43}N_3O_4$	533.709

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	852	1	000726235	9100-011	D 08	0.332	72.45	Spy4H	0.1776	TR0910000852	#NAME? 	$C_{32}H_{28}ClFN_2O_3$	543.035
9100	3731	1	000728874	9100-051	C 08	0.3	72.29	Spy4H	0.1776	TR0910003731	#NAME? 	$C_{37}H_{39}N_3O_4$	589.732
9100	3019	1	000728162	9100-042	C 09	0.205	72.18	Spy4H	0.1776	TR0910003019	#NAME? 	$C_{30}H_{43}N_3O_4$	509.687

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	860	1	000726243	9100-011	D 09	0.266	72.18	Spy4H	0.1776	TR0910000860	#NAME? 	$C_{31} H_{34} Cl N_3 O_3$	532.081
9100	1708	1	000726851	9100-023	D 05	0.379	72.09	Spy4H	0.1776	TR0910001708	#NAME? 	$C_{26} H_{33} Br N_2 O_4$	517.461
9100	2468	1	000727611	9100-035	D 10	0.28	71.54	Spy4H	0.1776	TR0910002468	#NAME? 	$C_{28} H_{37} Br N_2 O_4$	545.514
9100	2733	1	000727876	9100-039	E 03	0.429	71.19	Spy4H	0 1776	TR0910002733	#NAME? 	$C_{33} H_{30} Cl F N_2 O_4$	573.061

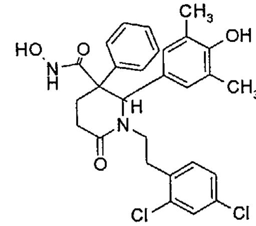
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1709	1	000726852	9100-023	E 05	0.383	71.02	Spy4H	0.1776	TR0910001709	#NAME?	$C_{28}H_{36}BrN_3O_3$	542.514
9100	842	1	000726225	9100-011	B 07	0.215	70.82	Spy4H	0.1776	TR0910000842	#NAME?	$C_{31}H_{34}ClN_3O_3$	532.081
9100	874	1	000726257	9100-011	B 11	0.256	70.82	Spy4H	0.1776	TR0910000874	#NAME?	$C_{28}H_{26}ClN_3O_3$	487.984
9100	1717	1	000726860	9100-023	E 06	0.329	70.21	Spy4H	0.1776	TR0910001717	#NAME?	$C_{22}H_{25}BrN_2O_4$	461.353

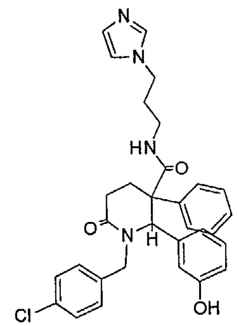
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1093	1	000726476	9100-014	E 08	0.307	70.04	Spy4H	0.1776	TR0910001093	#NAME?	$C_{28}H_{29}FN_2O_3$	460.546
9100	844	1	000726227	9100-011	D 07	0.221	69.74	Spy4H	0.1776	TR0910000844	#NAME?	$C_{30}H_{29}ClN_4O_3$	529.037
9100	1020	1	000726403	9100-013	D 09	0.217	69.72	Spy4H	0.1776	TR0910001020	#NAME?	$C_{30}H_{41}N_3O_3$	491.672
9100	2443	1	000727586	9100-035	C 07	0.383	69.62	Spy4H	0.1776	TR0910002443	#NAME?	$C_{28}H_{35}BrN_2O_3$	527.5

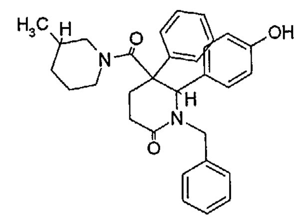
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	850	1	000726233	9100-011	B 08	0.322	69.47	Spy4H	0.1776	TR0910000850	#NAME?	$C_{30}H_{31}ClN_2O_4$	519.038
9100	851	1	000726234	9100-011	C 08	0.374	69.20	Spy4H	0.1776	TR0910000851	#NAME?	$C_{33}H_{31}ClN_2O_3$	539.072
9100	3733	1	000728876	9100-051	E 08	0.332	68.93	Spy4H	0.1776	TR0910003733	#NAME?	$C_{36}H_{36}FN_3O_4$	593.695

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID				
9100	981	1	000726364	9100-013	E 04	0.321	68.63	Spy4H	0.1776	TR0910000981	#NAME?	$C_{30}H_{38}BrN_3O_4$	584.551
9100	2739	1	000727882	9100-039	C 04	0.205	68.58	Spy4H	0.1776	TR0910002739	#NAME?	$C_{31}H_{36}ClN_3O_4$	550.095
9100	2749	1	000727892	9100-039	E 05	0.252	68.29	Spy4H	0.1776	TR0910002749	#NAME?	$C_{32}H_{36}ClN_3O_4$	562.106

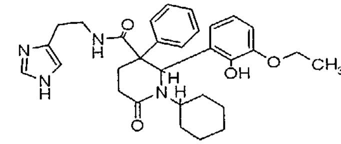
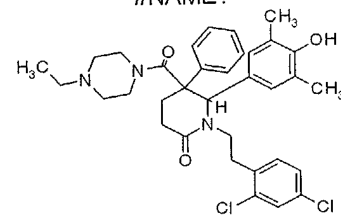
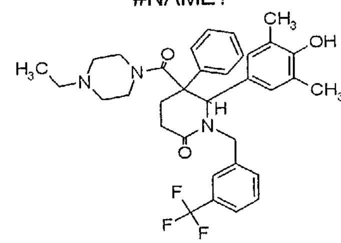
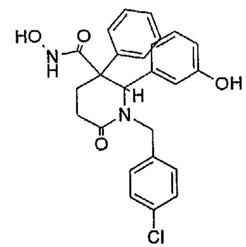
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2517	1	000727660	9100-036	E 06	0.402	68.27	Spy4H	0.1776	TR0910002517	#NAME?	$C_{28} H_{28} Cl_2 N_2 O_4$	527.445
9100	854	1	000726237	9100-011	F 08	0.269	67.85	Spy4H	0.1776	TR0910000854	#NAME?	$C_{31} H_{31} Cl N_4 O_3$	543.064
9100	1755	1	000726898	9100-023	C 11	0.363	67.80	Spy4H	0.1776	TR0910001755	#NAME?	$C_{31} H_{34} N_2 O_3$	482.621







Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2429	1	000727572	9100-035	E 05	0.217	67.70	Spy4H	0.1776	TR0910002429	#NAME?	$C_{33}H_{39}N_3O_3$	525.689
9100	1092	1	000726475	9100-014	D 08	0.322	67.49	Spy4H	0.1776	TR0910001092	#NAME?	$C_{28}H_{29}FN_2O_3$	460 546
9100	613	1	000725996	9100-008	E 08	0.319	67.40	Spy4H	0.1776	TR0910000613	#NAME?	$C_{28}H_{29}FN_2O_3$	460 546
9100	845	1	000726228	9100-011	E 07	0.421	67.31	Spy4H	0.1776	TR0910000845	#NAME?	$C_{30}H_{31}ClN_2O_3$	503.039

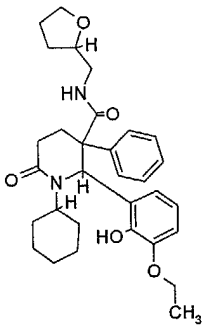
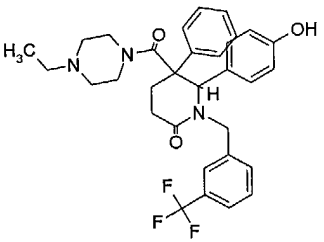
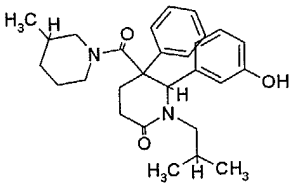
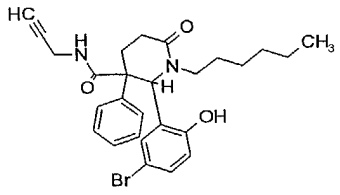
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID				
9100	2324	1	000727467	9100-033	D 02	0.232	66.94	Spy4H	0.1776	TR0910002324	#NAME?		$C_{31}H_{38}N_4O_4$	530.665
9100	2500	1	000727643	9100-036	D 04	0.368	66.93	Spy4H	0.1776	TR0910002500	#NAME?		$C_{34}H_{39}Cl_2N_3O_3$	608.606
9100	700	1	000726083	9100-009	D 09	0.288	66.86	Spy4H	0.1776	TR0910000700	#NAME?		$C_{34}H_{38}F_3N_3O_3$	593.686
9100	877	1	000726260	9100-011	E 11	0.255	66.77	Spy4H	0.1776	TR0910000877	#NAME?		$C_{25}H_{23}ClN_2O_4$	450.92

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2595	1	000727738	9100-037	C 06	0.24	66.62	Spy4H	0.1776	TR0910002595	#NAME?	$C_{36}H_{43}N_3O_3$	565.754
9100	1013	1	000726396	9100-013	E 08	0.414	66.46	Spy4H	0.1776	TR0910001013	#NAME?	$C_{31}H_{35}FN_2O_3$	502.626
9100	2731	1	000727874	9100-039	C 03	0.388	66.26	Spy4H	0.1776	TR0910002731	#NAME?	$C_{34}H_{33}ClN_2O_4$	569.098
9100	1710	1	000726853	9100-023	F 05	0.415	66.20	Spy4H	0.1776	TR0910001710	#NAME?	$C_{25}H_{27}BrN_2O_3$	483.403

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	662	1	000726045	9100-009	F 04	0.32	65.85	Spy4H	0.1776	TR0910000662	#NAME?	$C_{31}H_{34}Cl_2N_2O_4$	569.526
9100	731	1	000726114	9100-010	C 03	0.283	65 76	Spy4H	0.1776	TR0910000731	#NAME?	$C_{28}H_{30}N_2O_3$	442.556
9100	1702	1	000726845	9100-023	F 04	0.417	65.66	Spy4H	0.1776	TR0910001702	#NAME?	$C_{27}H_{35}BrN_2O_4$	531.487
9100	2355	1	000727498	9100-033	C 06	0.452	65.53	Spy4H	0.1776	TR0910002355	#NAME?	$C_{32}H_{42}N_2O_4$	518.694
9100	1955	1	000727098	9100-028	C 06	0.353	65.27	Spy4H	0.1776	TR0910001955	#NAME?	$C_{31}H_{40}N_2O_4$	504.667

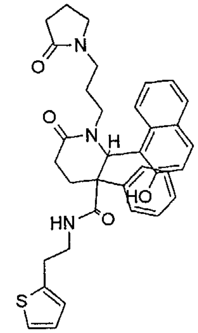
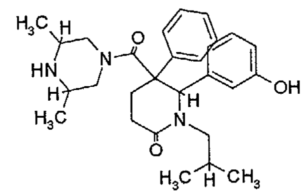
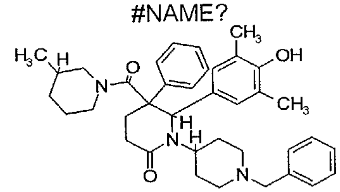
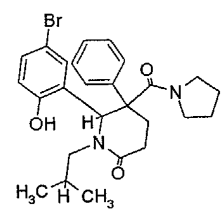
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2475	1	000727618	9100-035	C 11	0.305	65.13	Spy4H	0.1776	TR0910002475	#NAME?	$C_{30}H_{39}BrN_2O_3$	555.553
9100	971	1	000726354	9100-013	C 03	0.379	65.11	Spy4H	0.1776	TR0910000971	#NAME?	$C_{33}H_{36}BrN_3O_4$	618.568
9100	2531	1	000727674	9100-036	C 08	0.302	65.06	Spy4H	0.1776	TR0910002531	#NAME?	$C_{33}H_{40}N_2O_5$	544.688
9100	2533	1	000727676	9100-036	E 08	0.304	65.06	Spy4H	0.1776	TR0910002533	#NAME?	$C_{32}H_{37}FN_2O_5$	548 651

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	843	1	000726226	9100-011	C 07	0.364	64.87	Spy4H	0.1776	TR0910000843	#NAME?	$C_{29}H_{29}ClN_2O_3$	489.012
9100	2740	1	000727883	9100-039	D 04	0.384	64.80	Spy4H	0.1776	TR0910002740	#NAME?	$C_{32}H_{36}ClN_3O_4$	562.106
9100	612	1	000725995	9100-008	D 08	0.339	64.80	Spy4H	0.1776	TR0910000612	#NAME?	$C_{28}H_{29}FN_2O_3$	460.546
9100	237	1	000725620	9100-003	E 11	0.281	64.74	Spy4H	0.1776	TR0910000237	#NAME?	$C_{21}H_{21}BrN_2O_4$	445.311

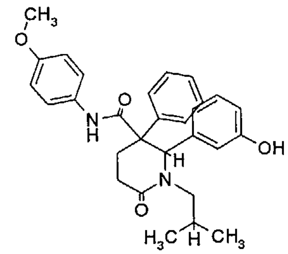
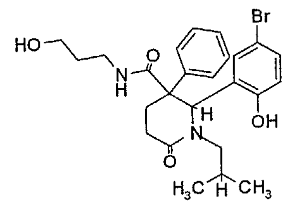
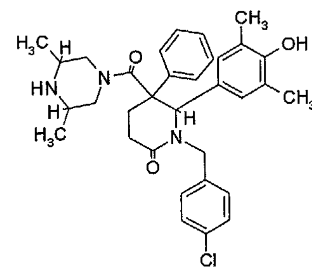
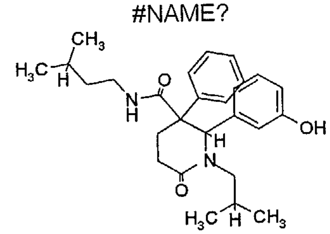
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2330	1	000727473	9100-033	B 03	0.281	64.69	Spy4H	0.1776	TR0910002330	#NAME?	$C_{31}H_{40}N_2O_5$	520.666
9100	4100	1	000729243	9100-057	D 04	0.261	64.67	Spy4H	0.1776	TR0910004100	 #NAME?	$C_{32}H_{34}F_3N_3O_3$	565.633
9100	595	1	000725978	9100-008	C 06	0.339	64.51	Spy4H	0.1776	TR0910000595	 #NAME?	$C_{28}H_{36}N_2O_3$	448.603
9100	2470	1	000727613	9100-035	F 10	0.294	64.49	Spy4H	0.1776	TR0910002470	 #NAME?	$C_{27}H_{31}BrN_2O_3$	511.457
													

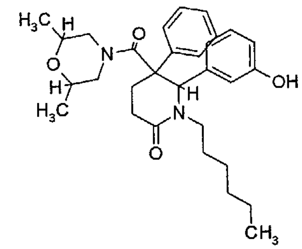
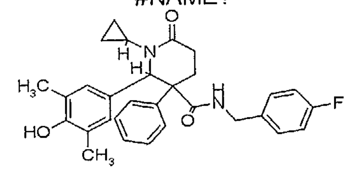
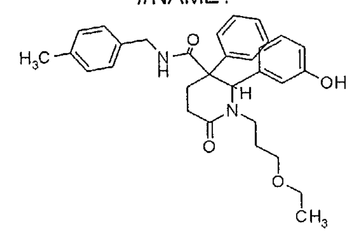
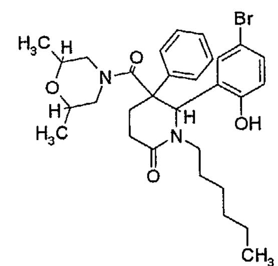
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	973	1	000726356	9100-013	E 03	0.304	64.02	Spy4H	0.1776	TR0910000973	#NAME?	$C_{32}H_{33}BrFN_3O_4$	622.532
9100	647	1	000726030	9100-009	G 02	0.295	63.83	Spy4H	0.1776	TR0910000647	#NAME?	$C_{29}H_{30}Cl_2N_2O_4$	541.472
9100	878	1	000726261	9100-011	F 11	0.356	63.79	Spy4H	0.1776	TR0910000878	#NAME?	$C_{31}H_{33}ClN_2O_4$	533.065
9100	573	1	000725956	9100-008	E 03	0.359	63.64	Spy4H	0.1776	TR0910000573	#NAME?	$C_{29}H_{31}FN_2O_3$	474.573

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2235	1	000727378	9100-031	C 11	0.239	63.59	Spy4H	0.1776	TR0910002235	#NAME?	$C_{36}H_{43}N_3O_3$	565.754
9100	2422	1	000727565	9100-035	F 04	0.259	63.53	Spy4H	0.1776	TR0910002422	#NAME?	$C_{32}H_{38}N_2O_4$	514.662
9100	847	1	000726230	9100-011	G 07	0.292	63.52	Spy4H	0.1776	TR0910000847	#NAME?	$C_{28}H_{29}ClN_2O_4$	493
9100	1014	1	000726397	9100-013	F 08	0.247	63.48	Spy4H	0.1776	TR0910001014	#NAME?	$C_{30}H_{38}N_4O_3$	502.655

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID				
9100	3751	1	000728894	9100-051	G 10	0.289	63.44	Spy4H	0.1776	TR0910003751	#NAME? 	$C_{35}H_{37}N_3O_4S$	595.76
9100	589	1	000725972	9100-008	E 05	0.225	63.35	Spy4H	0.1776	TR0910000589	#NAME? 	$C_{28}H_{37}N_3O_3$	463.618
9100	4155	1	000729298	9100-057	C 11	0.321	63.27	Spy4H	0.1776	TR0910004155	#NAME? 	$C_{38}H_{47}N_3O_3$	593.807
9100	1683	1	000726826	9100-023	C 02	0.484	63.25	Spy4H	0.1776	TR0910001683	#NAME? 	$C_{26}H_{31}BrN_2O_3$	499.446

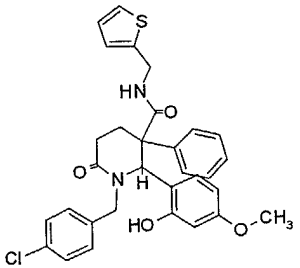
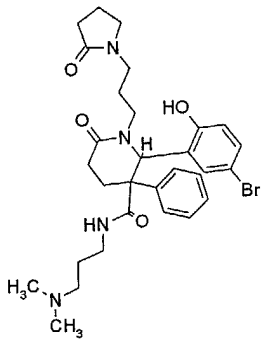
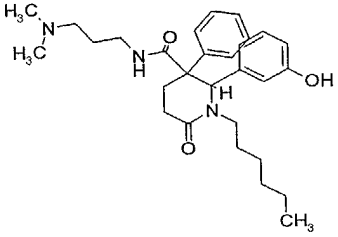
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	856	1	000726239	9100-011	H 08	0.335	63.25	Spy4H	0.1776	TR0910000856	#NAME?	$C_{28}H_{29}ClN_2O_3$	477.001
9100	865	1	000726248	9100-011	A 10	0.272	63.25	Spy4H	0.1776	TR0910000865	#NAME?	$C_{29}H_{31}ClN_2O_3S$	523.094
9100	1076	1	000726459	9100-014	D 06	0.291	63.24	Spy4H	0.1776	TR0910001076	#NAME?	$C_{30}H_{32}N_2O_4$	484.593
9100	2427	1	000727570	9100-035	C 05	0.268	63.21	Spy4H	0.1776	TR0910002427	#NAME?	$C_{30}H_{34}N_2O_4$	486.609

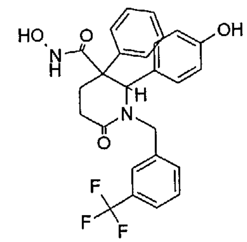
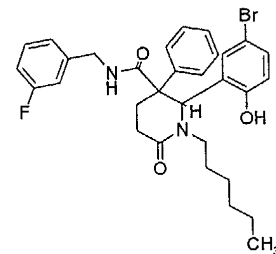
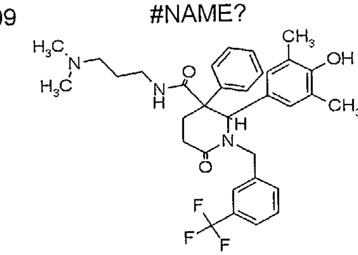
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	596	1	000725979	9100-008	D 06	0.286	63.06	Spy4H	0.1776	TR0910000596	#NAME? 	$C_{29} H_{32} N_2 O_4$	472.582
9100	1707	1	000726850	9100-023	C 05	0.352	62.99	Spy4H	0.1776	TR0910001707	#NAME? 	$C_{25} H_{31} Br N_2 O_4$	503.434
9100	2629	1	000727772	9100-037	E 10	0.275	62.89	Spy4H	0.1776	TR0910002629	#NAME? 	$C_{33} H_{38} Cl N_3 O_3$	560.134
9100	581	1	000725964	9100-008	E 04	0.326	62.77	Spy4H	0.1776	TR0910000581	#NAME? 	$C_{27} H_{36} N_2 O_3$	436.592

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1038	1	000726421	9100-013	F 11	0.295	62.40	Spy4H	0.1776	TR0910001038	#NAME? 	$C_{30}H_{40}N_2O_4$	492.656
9100	773	1	000726156	9100-010	E 08	0.231	62.39	Spy4H	0.1776	TR0910000773	#NAME? 	$C_{30}H_{31}FN_2O_3$	486.584
9100	1971	1	000727114	9100-028	C 08	0.296	61.99	Spy4H	0.1776	TR0910001971	#NAME? 	$C_{31}H_{36}N_2O_4$	500.635
9100	2478	1	000727621	9100-035	F 11	0.265	61.92	Spy4H	0.1776	TR0910002478	#NAME? 	$C_{30}H_{39}BrN_2O_4$	571.552

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1028	1	000726411	9100-013	D 10	0.257	61.86	Spy4H	0.1776	TR0910001028	#NAME?	$C_{28}H_{38}N_2O_4$	466.618
9100	1045	1	000726428	9100-014	E 02	0.331	61.83	Spy4H	0.1776	TR0910001045	#NAME?	$C_{28}H_{34}N_2O_3$	446.588
9100	1091	1	000726474	9100-014	C 08	0.346	61.83	Spy4H	0.1776	TR0910001091	#NAME?	$C_{29}H_{32}N_2O_3$	456.583
9100	230	1	000725613	9100-003	F 10	0.323	61.69	Spy4H	0.1776	TR0910000230	#NAME?	$C_{24}H_{23}BrN_2O_3$	467.361

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	855	1	000726238	9100-011	G 08	0.344	61.63	Spy4H	0.1776	TR0910000855	#NAME?	$C_{28}H_{27}ClN_2O_3$	474.985
9100	3741	1	000728884	9100-051	E 09	0.246	61.60	Spy4H	0.1776	TR0910003741	#NAME?	$C_{34}H_{41}N_3O_4$	555.715
9100	2213	1	000727356	9100-031	E 08	0.271	61.41	Spy4H	0.1776	TR0910002213	#NAME?	$C_{37}H_{38}FN_3O_3$	591.723

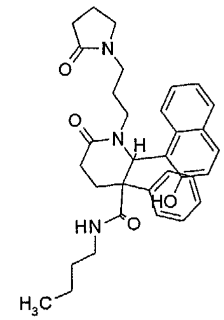
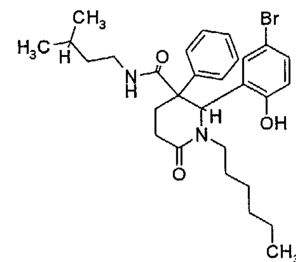
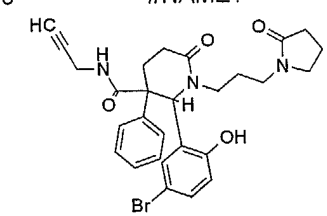
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID				
9100	2738	1	000727881	9100-039	B 04	0.398	61.32	Spy4H	0.1776	TR0910002738		#NAME?	$C_{31}H_{29}ClN_2O_4S$	561.099
9100	979	1	000726362	9100-013	C 04	0.245	61.31	Spy4H	0.1776	TR0910000979		#NAME?	$C_{30}H_{39}BrN_4O_4$	599.566
9100	1019	1	000726402	9100-013	C 09	0.239	61.31	Spy4H	0.1776	TR0910001019		#NAME?	$C_{29}H_{41}N_3O_3$	479.661

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	4117	1	000729260	9100-057	E 06	0.279	61.30	Spy4H	0.1776	TR0910004117	#NAME? 	$C_{26} H_{23} F_3 N_2 O_4$	484.472
9100	2452	1	000727595	9100-035	D 08	0.327	61.28	Spy4H	0.1776	TR0910002452	#NAME? 	$C_{31} H_{34} Br F N_2 O_3$	581.523
9100	699	1	000726082	9100-009	C 09	0.215	61.13	Spy4H	0.1776	TR0910000699	#NAME? 	$C_{33} H_{38} F_3 N_3 O_3$	581.675

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1756	1	000726899	9100-023	D 11	0.289	61.11	Spy4H	0.1776	TR0910001756	#NAME?	$C_{32}H_{30}N_2O_4$	506.599
9100	1002	1	000726385	9100-013	B 07	0.24	61.04	Spy4H	0.1776	TR0910001002	#NAME?	$C_{30}H_{41}N_3O_3$	491.672
9100	1004	1	000726387	9100-013	D 07	0.242	61.04	Spy4H	0.1776	TR0910001004	#NAME?	$C_{29}H_{36}N_4O_3$	488.628

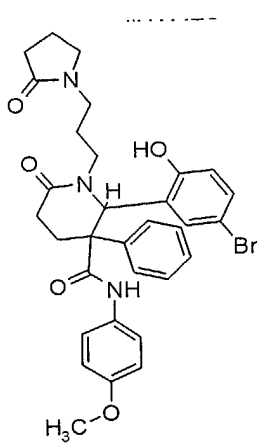
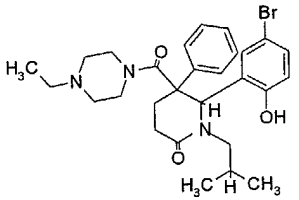
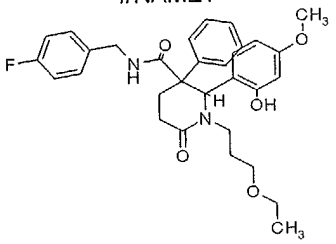
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	621	1	000726004	9100-008	E 09	0.29	61.03	Spy4H	0.1776	TR0910000621	#NAME?	$C_{26}H_{34}N_2O_3$	422.566
9100	2221	1	000727364	9100-031	E 09	0.251	60.87	Spy4H	0 1776	TR0910002221	#NAME?	$C_{35}H_{43}N_3O_3$	553.743
9100	689	1	000726072	9100-009	A 08	0.249	60.79	Spy4H	0.1776	TR0910000689	#NAME?	$C_{33}H_{36}F_3N_3O_3$	579.659
9100	2322	1	000727465	9100-033	B 02	0.255	60.75	Spy4H	0.1776	TR0910002322	#NAME?	$C_{32}H_{43}N_3O_4$	533.709
9100	2969	1	000728112	9100-042	A 03	0.328	60.74	Spy4H	0.1776	TR0910002969	#NAME?	$C_{31}H_{33}Cl_2N_3O_3$	566.526

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	849	1	000726232	9100-011	A 08	0.295	60.55	Spy4H	0.1776	TR0910000849	#NAME?	$C_{30}H_{32}ClN_3O_3$	518.054
9100	866	1	000726249	9100-011	B 10	0 398	60.55	Spy4H	0.1776	TR0910000866	#NAME?	$C_{29}H_{31}ClN_2O_3$	491.028
9100	873	1	000726256	9100-011	A 11	0.371	60.55	Spy4H	0.1776	TR0910000873	#NAME?	$C_{29}H_{31}ClN_2O_4$	507.027
9100	605	1	000725988	9100-008	E 07	0.254	60.46	Spy4H	0.1776	TR0910000605	#NAME?	$C_{26}H_{32}N_2O_3$	420.55

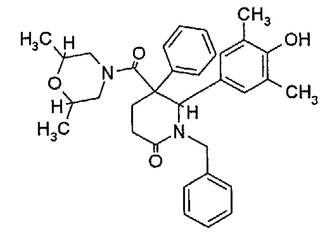
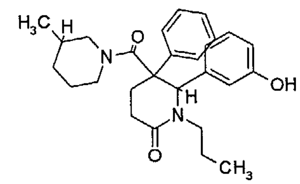
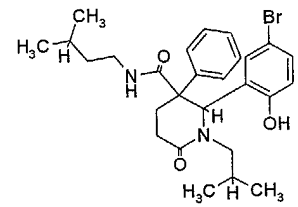
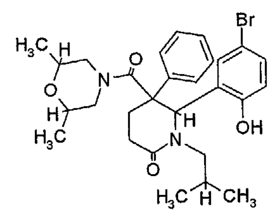
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3752	1	000728895	9100-051	H 10	0.258	60.38	Spy4H	0.1776	TR0910003752	#NAME? 	$C_{33}H_{39}N_3O_4$	541.688
9100	2461	1	000727604	9100-035	E 09	0.402	60.32	Spy4H	0.1776	TR0910002461	#NAME? 	$C_{29}H_{39}BrN_2O_3$	543.542
9100	990	1	000726373	9100-013	F 05	0.26	60.23	Spy4H	0.1776	TR0910000990	#NAME? 	$C_{28}H_{30}BrN_3O_4$	552.466

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	711	1	000726094	9100-009	G 10	0.388	60.12	Spy4H	0.1776	TR0910000711	#NAME?	$C_{34}H_{33}F_3N_2O_3S$	606.706
9100	2436	1	000727579	9100-035	D 06	0.314	60.00	Spy4H	0.1776	TR0910002436	#NAME?	$C_{34}H_{34}N_2O_4$	534.653
9100	2339	1	000727482	9100-033	C 04	0.257	59.91	Spy4H	0.1776	TR0910002339	#NAME?	$C_{31}H_{43}N_3O_4$	521.698
9100	572	1	000725955	9100-008	D 03	0.338	59.88	Spy4H	0.1776	TR0910000572	#NAME?	$C_{29}H_{31}FN_2O_3$	474 573

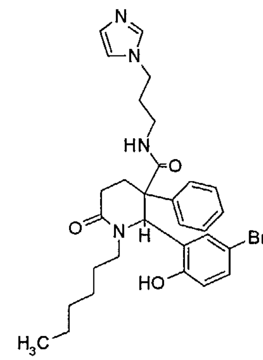
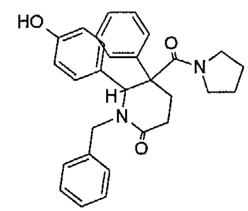
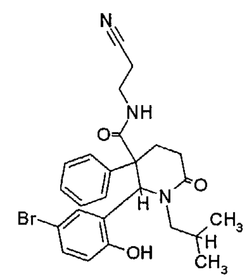
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1061	1	000726444	9100-014	E 04	0.403	59.84	Spy4H	0.1776	TR0910001061	#NAME?	$C_{28}H_{36}N_2O_3$	448.603
9100	857	1	000726240	9100-011	A 09	0.265	59.74	Spy4H	0.1776	TR0910000857	#NAME?	$C_{27}H_{27}ClN_2O_4$	478.973
9100	861	1	000726244	9100-011	E 09	0.427	59.74	Spy4H	0.1776	TR0910000861	#NAME?	$C_{30}H_{33}ClN_2O_3$	505.055
9100	2637	1	000727780	9100-037	E 11	0.35	59.73	Spy4H	0 1776	TR0910002637	#NAME?	$C_{27}H_{27}ClN_2O_4$	478.973

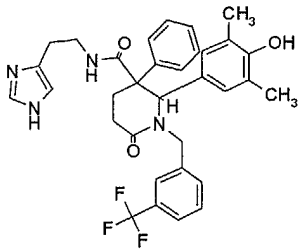
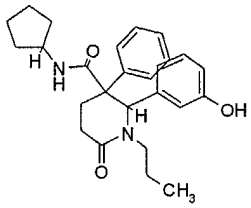
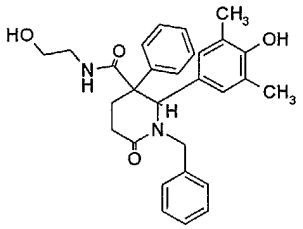
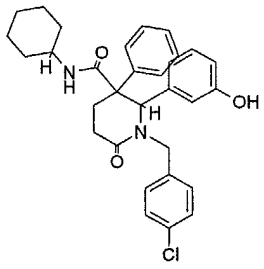
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	996	1	000726379	9100-013	D 06	0.279	59.69	Spy4H	0.1776	TR0910000996		$C_{32}H_{34}BrN_3O_5$	620.541
9100	1700	1	000726843	9100-023	D 04	0.316	59.50	Spy4H	0.1776	TR0910001700	#NAME? 	$C_{28}H_{36}BrN_3O_3$	542.514
9100	813	1	000726196	9100-011	E 03	0.38	59.47	Spy4H	0.1776	TR0910000813	#NAME? 	$C_{31}H_{35}FN_2O_5$	534.625

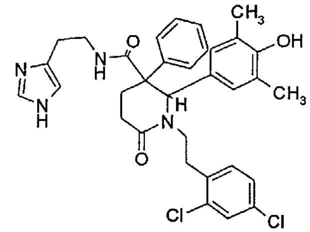
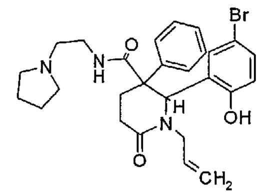
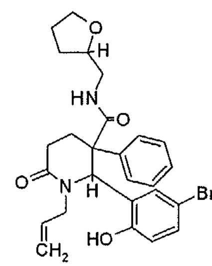
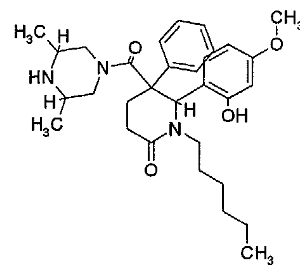
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2489	1	000727632	9100-036	A 03	0.361	59.45	Spy4H	0.1776	TR0910002489	#NAME?	$C_{33}H_{37}Cl_2N_3O_3$	594.579
9100	988	1	000726371	9100-013	D 05	0.247	59.42	Spy4H	0.1776	TR0910000988	#NAME?	$C_{29}H_{36}BrN_3O_5$	586.523
9100	3236	1	000728379	9100-045	D 06	0.304	59.42	Spy4H	0 1776	TR0910003236	#NAME?	$C_{30}H_{32}N_2O_4$	484.593

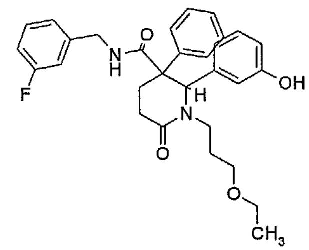
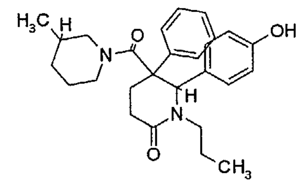
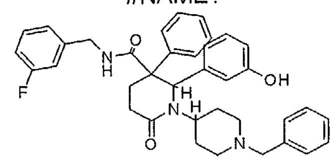
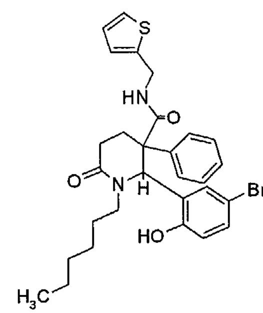
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2438	1	000727581	9100-035	F 06	0.285	59.36	Spy4H	0.1776	TR0910002438	#NAME? 	$C_{33} H_{38} N_2 O_4$	526.673
9100	1115	1	000726498	9100-014	C 11	0.262	59.28	Spy4H	0.1776	TR0910001115	#NAME? 	$C_{27} H_{34} N_2 O_3$	434.577
9100	1701	1	000726844	9100-023	E 04	0.512	59.24	Spy4H	0.1776	TR0910001701	#NAME? 	$C_{27} H_{35} Br N_2 O_3$	515.489
9100	1718	1	000726861	9100-023	F 06	0.364	59.24	Spy4H	0.1776	TR0910001718	#NAME? 	$C_{28} H_{35} Br N_2 O_4$	543.498

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1733	1	000726876	9100-023	E 08	0.331	59.24	Spy4H	0.1776	TR0910001733	#NAME?	$C_{32}H_{29}FN_2O_3$	508.59
9100	835	1	000726218	9100-011	C 06	0.321	59.20	Spy4H	0.1776	TR0910000835	#NAME?	$C_{30}H_{40}N_2O_5$	508.655
9100	1022	1	000726405	9100-013	F 09	0.261	59.15	Spy4H	0.1776	TR0910001022	#NAME?	$C_{29}H_{40}N_2O_4$	480.645

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2454	1	000727597	9100-035	F 08	0.283	59.04	Spy4H	0.1776	TR0910002454	#NAME?	$C_{30}H_{37}BrN_4O_3$	581.551
													
9100	1723	1	000726866	9100-023	C 07	0.289	58.97	Spy4H	0.1776	TR0910001723	#NAME?	$C_{29}H_{30}N_2O_3$	454.567
													
9100	1714	1	000726857	9100-023	B 06	0.335	58.70	Spy4H	0.1776	TR0910001714	#NAME?	$C_{25}H_{28}BrN_3O_3$	498.418
													

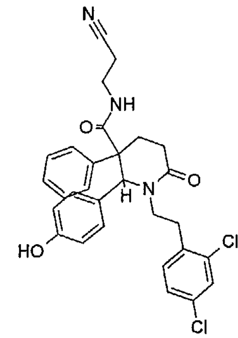
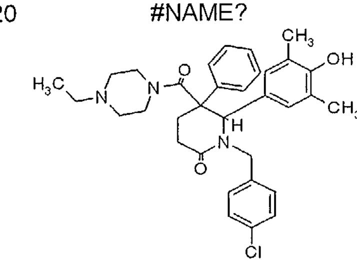
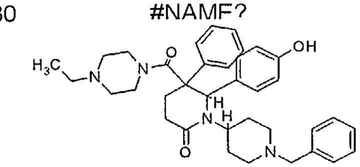
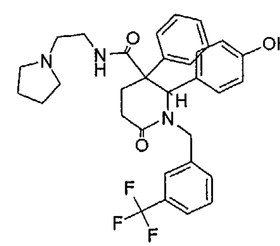
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	684	1	000726067	9100-009	D 07	0.231	58.43	Spy4H	0.1776	TR0910000684	#NAME?	$C_{33}H_{33}F_3N_4O_3$	590.643
													
9100	1085	1	000726468	9100-014	E 07	0.26	58.43	Spy4H	0.1776	TR0910001085	#NAME?	$C_{26}H_{32}N_2O_3$	420.55
													
9100	2417	1	000727560	9100-035	A 04	0.302	58.40	Spy4H	0.1776	TR0910002417	#NAME?	$C_{29}H_{32}N_2O_4$	472.582
													
9100	848	1	000726231	9100-011	H 07	0.279	58.38	Spy4H	0.1776	TR0910000848	#NAME?	$C_{31}H_{33}ClN_2O_3$	517.066
													

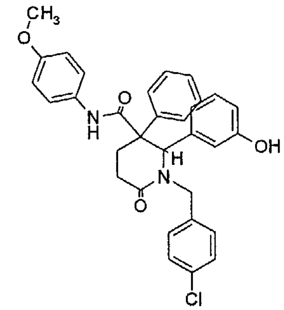
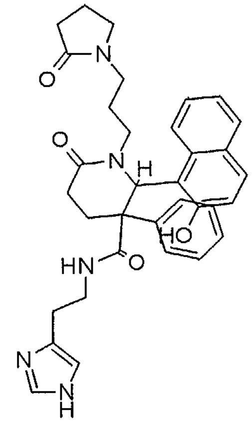
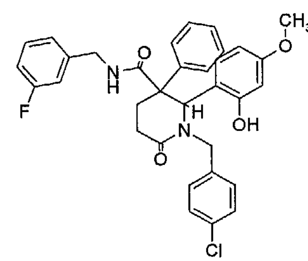
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2484	1	000727627	9100-036	D 02	0.319	58.38	Spy4H	0.1776	TR0910002484	#NAME?	$C_{33}H_{34}Cl_2N_4O_3$	605.563
													
9100	202	1	000725585	9100-003	B 07	0.243	58.34	Spy4H	0.1776	TR0910000202	#NAME?	$C_{27}H_{32}BrN_3O_3$	526.472
													
9100	210	1	000725593	9100-003	B 08	0.331	58.34	Spy4H	0.1776	TR0910000210	#NAME?	$C_{26}H_{29}BrN_2O_4$	513.429
													
9100	3029	1	000728172	9100-042	E 10	0.279	58.29	Spy4H	0.1776	TR0910003029	#NAME?	$C_{31}H_{43}N_3O_4$	521.698
													

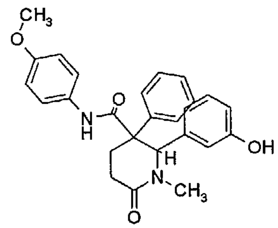
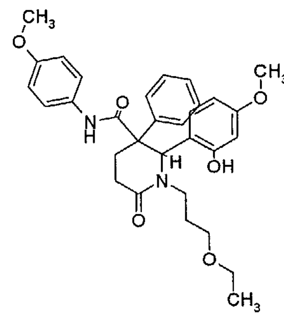
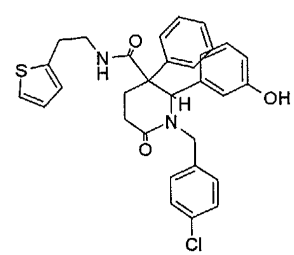
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1972	1	000727115	9100-028	D 08	0.284	58.15	Spy4H	0.1776	TR0910001972	#NAME? 	$C_{30}H_{33}FN_2O_4$	504.599
9100	635	1	000726018	9100-008	C 11	0.326	58.14	Spy4H	0.1776	TR0910000635	#NAME? 	$C_{27}H_{34}N_2O_3$	434.577
9100	2212	1	000727355	9100-031	D 08	0.281	58.14	Spy4H	0.1776	TR0910002212	#NAME? 	$C_{37}H_{38}FN_3O_3$	591.723
9100	2458	1	000727601	9100-035	B 09	0 285	58 08	Spy4H	0.1776	TR0910002458	#NAME? 	$C_{29}H_{33}BrN_2O_3S$	569.561

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	980	1	000726363	9100-013	D 04	0.254	58.06	Spy4H	0.1776	TR0910000980	#NAME?	$C_{31}H_{39}BrN_4O_4$	611.577
9100	2446	1	000727589	9100-035	F 07	0.408	57.76	Spy4H	0.1776	TR0910002446	#NAME?	$C_{27}H_{33}BrN_2O_3$	513.473
9100	2465	1	000727608	9100-035	A 10	0.25	57.76	Spy4H	0.1776	TR0910002465	#NAME?	$C_{28}H_{37}BrN_2O_3S$	561.581

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3732	1	000728875	9100-051	D 08	0.312	57.63	Spy4H	0.1776	TR0910003732	#NAME?	$C_{36}H_{36}FN_3O_4$	593.695
9100	2435	1	000727578	9100-035	C 06	0.395	57.43	Spy4H	0.1776	TR0910002435	#NAME?	$C_{33}H_{38}N_2O_3$	510.674
9100	811	1	000726194	9100-011	C 03	0.377	57.30	Spy4H	0.1776	TR0910000811	#NAME?	$C_{32}H_{38}N_2O_5$	530.661

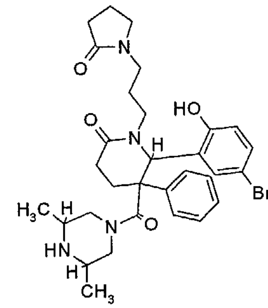
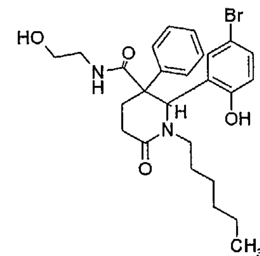
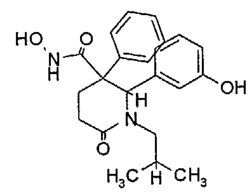
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2994	1	000728137	9100-042	B 06	0.413	57.20	Spy4H	0.1776	TR0910002994	#NAME? 	$C_{29}H_{27}Cl_2N_3O_3$	536.456
9100	2620	1	000727763	9100-037	D 09	0.268	57.14	Spy4H	0.1776	TR0910002620	#NAME? 	$C_{33}H_{38}ClN_3O_3$	560.134
9100	2580	1	000727723	9100-037	D 04	0.243	56.86	Spy4H	0.1776	TR0910002580	#NAME? 	$C_{36}H_{44}N_4O_3$	580.769
9100	4082	1	000729225	9100-057	B 02	0.248	56.80	Spy4H	0.1776	TR0910004082	#NAME? 	$C_{32}H_{34}F_3N_3O_3$	565.633

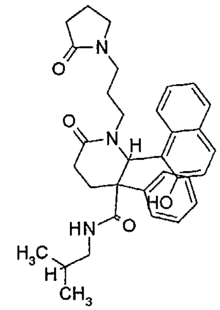
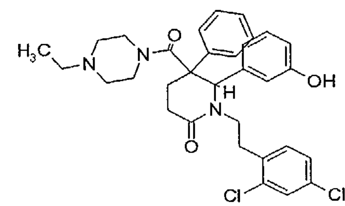
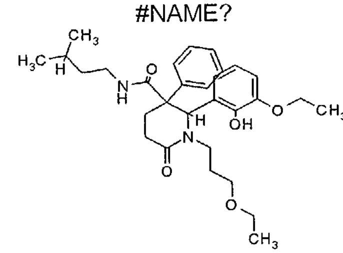
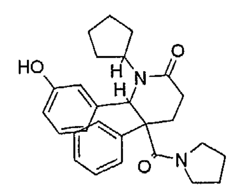
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	876	1	000726259	9100-011	D 11	0.432	56.76	Spy4H	0.1776	TR0910000876	#NAME? 	$C_{32}H_{29}ClN_2O_4$	541.044
9100	3724	1	000728867	9100-051	D 07	0.252	56.72	Spy4H	0.1776	TR0910003724		$C_{34}H_{37}N_5O_4$	579.697
9100	2732	1	000727875	9100-039	D 03	0.457	56.68	Spy4H	0.1776	TR0910002732	#NAME? 	$C_{33}H_{30}ClFN_2O_4$	573.061

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	196	1	000725579	9100-003	D 06	0.252	56.51	Spy4H	0.1776	TR0910000196	#NAME?	$C_{26} H_{26} N_2 O_4$	430.501
													
9100	836	1	000726219	9100-011	D 06	0.304	56.49	Spy4H	0.1776	TR0910000836	#NAME?	$C_{31} H_{36} N_2 O_6$	532.633
													
9100	871	1	000726254	9100-011	G 10	0.336	56.49	Spy4H	0.1776	TR0910000871	#NAME?	$C_{31} H_{29} Cl N_2 O_3 S$	545.1
													

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2453	1	000727596	9100-035	E 08	0.43	56.47	Spy4H	0.1776	TR0910002453	#NAME?	$C_{31}H_{34}BrFN_2O_3$	581.523
9100	1053	1	000726436	9100-014	E 03	0.478	56.44	Spy4H	0.1776	TR0910001053	#NAME?	$C_{30}H_{31}FN_2O_3$	486.584
9100	1116	1	000726499	9100-014	D 11	0.265	56.44	Spy4H	0.1776	TR0910001116	#NAME?	$C_{28}H_{30}N_2O_4$	458.555
9100	997	1	000726380	9100-013	E 06	0.254	56.44	Spy4H	0.1776	TR0910000997	#NAME?	$C_{25}H_{28}BrN_3O_5$	530.416

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	565	1	000725948	9100-008	E 02	0.304	56.40	Spy4H	0.1776	TR0910000565	#NAME?	$C_{27}H_{34}N_2O_3$	434.577
9100	2750	1	000727893	9100-039	F 05	0 457	56.39	Spy4H	0.1776	TR0910002750	#NAME?	$C_{29}H_{27}ClN_2O_4$	502.995
9100	821	1	000726204	9100-011	E 04	0.322	56.22	Spy4H	0.1776	TR0910000821	#NAME?	$C_{29}H_{40}N_2O_5$	496.644

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	989	1	000726372	9100-013	E 05	0.257	56.17	Spy4H	0.1776	TR0910000989	#NAME?	$C_{31}H_{39}BrN_4O_4$	611.577
													
9100	2457	1	000727600	9100-035	A 09	0.275	56.15	Spy4H	0.1776	TR0910002457	#NAME?	$C_{26}H_{33}BrN_2O_4$	517.461
													
9100	597	1	000725980	9100-008	E 06	0.25	56.11	Spy4H	0.1776	TR0910000597	#NAME?	$C_{22}H_{26}N_2O_4$	382.457
													

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3746	1	000728889	9100-051	B 10	0.268	56.11	Spy4H	0.1776	TR0910003746	#NAME? 	$C_{33} H_{39} N_3 O_4$	541.688
9100	660	1	000726043	9100-009	D 04	0.433	56.07	Spy4H	0.1776	TR0910000660	#NAME? 	$C_{32} H_{35} Cl_2 N_3 O_3$	580.552
9100	2541	1	000727684	9100-036	E 09	0.289	55.98	Spy4H	0.1776	TR0910002541	#NAME? 	$C_{30} H_{42} N_2 O_5$	510.671
9100	3203	1	000728346	9100-045	C 02	0.392	55.92	Spy4H	0.1776	TR0910003203	#NAME? 	$C_{27} H_{32} N_2 O_3$	432.561

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	987	1	000726370	9100-013	C 05	0.265	55.89	Spy4H	0.1776	TR0910000987	#NAME?	$C_{28}H_{34}BrN_3O_5$	572.497
9100	2403	1	000727546	9100-035	C 02	0.434	55.83	Spy4H	0.1776	TR0910002403	#NAME?	$C_{31}H_{34}N_2O_3$	482.621
9100	3721	1	000728864	9100-051	A 07	0.298	55.80	Spy4H	0.1776	TR0910003721	#NAME?	$C_{35}H_{40}N_4O_5$	596.724

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3738	1	000728881	9100-051	B 09	0.275	55.80	Spy4H	0.1776	TR0910003738	#NAME?	$C_{34}H_{35}N_3O_4S$	581.734
9100	2596	1	000727739	9100-037	D 06	0.263	55.71	Spy4H	0.1776	TR0910002596	#NAME?	$C_{37}H_{39}N_3O_4$	589.732
9100	3221	1	000728364	9100-045	E 04	0.375	55.66	Spy4H	0.1776	TR0910003221	#NAME?	$C_{28}H_{36}N_2O_3$	448.603

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3235	1	000728378	9100-045	C 06	0.352	55.66	Spy4H	0.1776	TR0910003235	#NAME?	$C_{29}H_{36}N_2O_3$	460.614
9100	3722	1	000728865	9100-051	B 07	0 26	55.50	Spy4H	0 1776	TR0910003722	#NAME?	$C_{35}H_{42}N_4O_4$	582.741
9100	702	1	000726085	9100-009	F 09	0.29	55.40	Spy4H	0.1776	TR0910000702	#NAME?	$C_{33}H_{37}F_3N_2O_4$	582.659
9100	1051	1	000726434	9100-014	C 03	0.422	55.31	Spy4H	0.1776	TR0910001051	#NAME?	$C_{31}H_{34}N_2O_3$	482.621

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1070	1	000726453	9100-014	F 05	0.255	55.31	Spy4H	0.1776	TR0910001070	#NAME?	$C_{26}H_{28}N_2O_3$	416.518
9100	1078	1	000726461	9100-014	F 06	0.255	55.31	Spy4H	0.1776	TR0910001078	#NAME?	$C_{29}H_{36}N_2O_4$	476.613
9100	3725	1	000728868	9100-051	E 07	0.264	55.19	Spy4H	0.1776	TR0910003725	#NAME?	$C_{34}H_{39}N_3O_4$	553.699

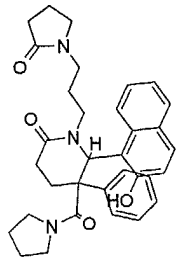
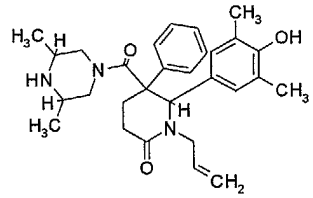
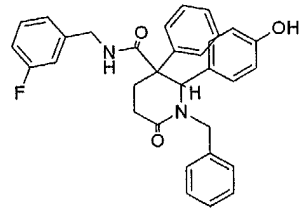
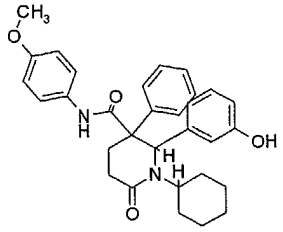
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3729	1	000728872	9100-051	A 08	0.301	55.19	Spy4H	0.1776	TR0910003729	#NAME?	$C_{34}H_{40}N_4O_4$	568.714
9100	3744	1	000728887	9100-051	H 09	0.268	55.19	Spy4H	0.1776	TR0910003744	#NAME?	$C_{34}H_{41}N_3O_4$	555.715
9100	2473	1	000727616	9100-035	A 11	0.334	55.19	Spy4H	0.1776	TR0910002473	#NAME?	$C_{28}H_{37}BrN_2O_4$	545.514

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1973	1	000727116	9100-028	E 08	0.28	55.14	Spy4H	0.1776	TR0910001973	#NAME?	$C_{30}H_{33}FN_2O_4$	504.599
9100	1005	1	000726388	9100-013	E 07	0.445	55.08	Spy4H	0.1776	TR0910001005	#NAME?	$C_{29}H_{38}N_2O_3$	462.63
9100	1066	1	000726449	9100-014	B 05	0.305	55.03	Spy4H	0.1776	TR0910001066	#NAME?	$C_{27}H_{34}N_2O_3$	434 577
9100	863	1	000726246	9100-011	G 09	0.487	54.87	Spy4H	0.1776	TR0910000863	#NAME? Chiral	$C_{33}H_{37}ClN_2O_3$	545.119

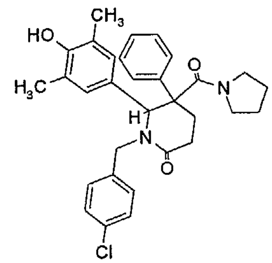
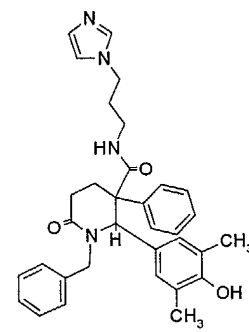
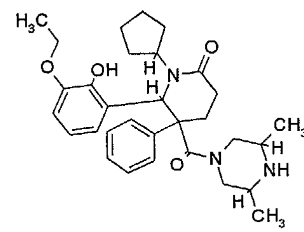
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1052	1	000726435	9100-014	D 03	0.419	54.75	Spy4H	0.1776	TR0910001052	#NAME?	$C_{30}H_{31}FN_2O_3$	486.584
9100	1077	1	000726460	9100-014	E 06	0.257	54.75	Spy4H	0.1776	TR0910001077	#NAME?	$C_{23}H_{26}N_2O_4$	394.468
9100	206	1	000725589	9100-003	F 07	0.305	54.68	Spy4H	0.1776	TR0910000206	#NAME?	$C_{24}H_{25}BrN_2O_3$	469.376
9100	2404	1	000727547	9100-035	D 02	0.242	54.55	Spy4H	0.1776	TR0910002404	#NAME?	$C_{32}H_{34}N_4O_3$	522.646

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	687	1	000726070	9100-009	G 07	0.351	54.38	Spy4H	0.1776	TR0910000687	#NAME?	$C_{31}H_{33}F_3N_2O_4$	554.606
9100	704	1	000726087	9100-009	H 09	0.399	54.38	Spy4H	0.1776	TR0910000704	#NAME?	$C_{33}H_{37}F_3N_2O_3$	566.66
9100	3758	1	000728901	9100-051	F 11	0.285	54.27	Spy4H	0.1776	TR0910003758	#NAME?	$C_{35}H_{41}N_3O_5$	583.725
9100	1062	1	000726445	9100-014	F 04	0.258	54.18	Spy4H	0.1776	TR0910001062	#NAME?	$C_{28}H_{36}N_2O_4$	464.602

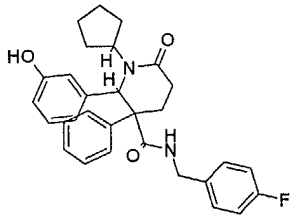
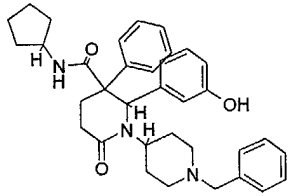
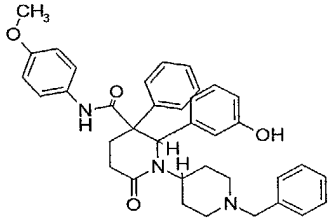
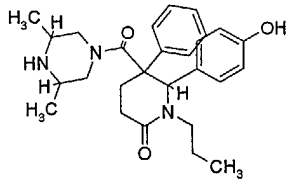
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1694	1	000726837	9100-023	F 03	0.304	54.15	Spy4H	0.1776	TR0910001694	#NAME?	$C_{28}H_{33}BrN_4O_3$	553.498
9100	2525	1	000727668	9100-036	E 07	0.325	54.11	Spy4H	0.1776	TR0910002525	#NAME?	$C_{30}H_{40}N_2O_5$	508.655
9100	2742	1	000727885	9100-039	F 04	0.4	54.06	Spy4H	0.1776	TR0910002742	#NAME?	$C_{31}H_{35}ClN_2O_5$	551 08
9100	2211	1	000727354	9100-031	C 08	0.323	54.05	Spy4H	0.1776	TR0910002211	#NAME?	$C_{38}H_{41}N_3O_3$	587.76

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID				
9100	3723	1	000728866	9100-051	C 07	0.28	53.97	Spy4H	0.1776	TR0910003723		#NAME?	$C_{33}H_{37}N_3O_4$	539.672
9100	1069	1	000726452	9100-014	E 05	0.259	53.90	Spy4H	0.1776	TR0910001069		#NAME?	$C_{29}H_{37}N_3O_3$	475.629
9100	1732	1	000726875	9100-023	D 08	0.333	53.88	Spy4H	0.1776	TR0910001732		#NAME?	$C_{32}H_{29}FN_2O_3$	508.59
9100	4396	1	000729539	9100-060	D 11	0.347	53.87	Spy4H	0.1776	TR0910004396		#NAME?	$C_{31}H_{34}N_2O_4$	498.62

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	571	1	000725954	9100-008	C 03	0.395	53.80	Spy4H	0.1776	TR0910000571	#NAME?	$C_{30}H_{34}N_2O_3$	470.61
9100	636	1	000726019	9100-008	D 11	0.278	53.80	Spy4H	0 1776	TR0910000636	#NAME?	$C_{28}H_{30}N_2O_4$	458.555
9100	3253	1	000728396	9100-045	E 08	0 283	53.78	Spy4H	0.1776	TR0910003253	#NAME?	$C_{30}H_{32}FN_3O_5$	533.597
9100	708	1	000726091	9100-009	D 10	0.306	53.71	Spy4H	0.1776	TR0910000708	#NAME?	$C_{32}H_{35}F_3N_2O_4$	568.633

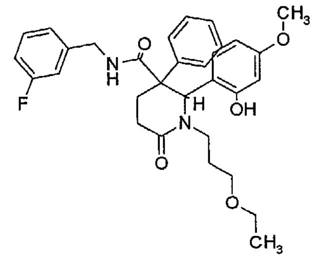
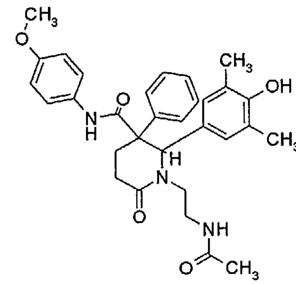
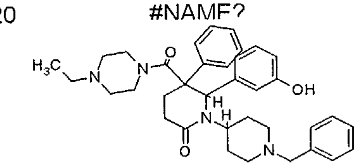
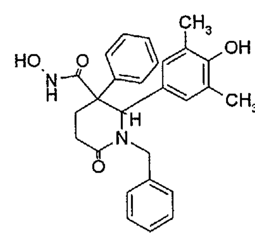
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2603	1	000727746	9100-037	C 07	0.467	53.70	Spy4H	0.1776	TR0910002603	#NAME?	$C_{31}H_{33}ClN_2O_3$	517.066
													
9100	2414	1	000727557	9100-035	F 03	0.258	53.59	Spy4H	0 1776	TR0910002414	#NAME?	$C_{33}H_{36}N_4O_3$	536 672
													
9100	1949	1	000727092	9100-028	E 05	0.281	53.49	Spy4H	0.1776	TR0910001949	#NAME?	$C_{31}H_{41}N_3O_4$	519.682
													

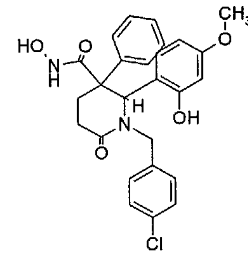
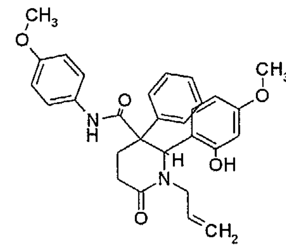
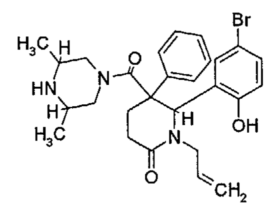
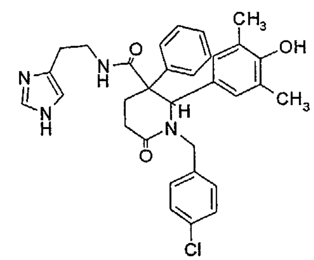
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	998	1	000726381	9100-013	F 06	0.276	53.46	Spy4H	0.1776	TR0910000998	#NAME?	$C_{31}H_{38}BrN_3O_5$	612.561
9100	765	1	000726148	9100-010	E 07	0.252	53.41	Spy4H	0.1776	TR0910000765	#NAME?	$C_{28}H_{34}N_2O_3$	446.588
9100	3756	1	000728899	9100-051	D 11	0.288	53.36	Spy4H	0.1776	TR0910003756		$C_{36}H_{37}N_3O_5$	591.704

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3213	1	000728356	9100-045	E 03	0.422	53.24	Spy4H	0.1776	TR0910003213	#NAME?	$C_{30}H_{31}FN_2O_3$	486.584
													
9100	2205	1	000727348	9100-031	E 07	0.27	53.24	Spy4H	0.1776	TR0910002205	#NAME?	$C_{35}H_{41}N_3O_3$	551.727
													
9100	2236	1	000727379	9100-031	D 11	0.276	53.24	Spy4H	0.1776	TR0910002236	#NAME?	$C_{37}H_{39}N_3O_4$	589.732
													
9100	629	1	000726012	9100-008	E 10	0 258	53.22	Spy4H	0.1776	TR0910000629	#NAME?	$C_{27}H_{35}N_3O_3$	449.591
													

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1058	1	000726441	9100-014	B 04	0.351	53.05	Spy4H	0.1776	TR0910001058	#NAME?	$C_{28}H_{30}N_2O_3S$	474.622
9100	1068	1	000726451	9100-014	D 05	0.261	53.05	Spy4H	0.1776	TR0910001068	#NAME?	$C_{27}H_{34}N_2O_4$	450.576
9100	598	1	000725981	9100-008	F 06	0.264	52.93	Spy4H	0.1776	TR0910000598	#NAME?	$C_{28}H_{36}N_2O_4$	464.602
9100	2573	1	000727716	9100-037	E 03	0.287	52.84	Spy4H	0.1776	TR0910002573	#NAME?	$C_{37}H_{38}FN_3O_3$	591.723

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1086	1	000726469	9100-014	F 07	0.263	52.76	Spy4H	0.1776	TR0910001086	#NAME?	$C_{24}H_{28}N_2O_3$	392.496
9100	1098	1	000726481	9100-014	B 09	0.298	52.76	Spy4H	0.1776	TR0910001098		$C_{26}H_{28}N_2O_3S$	448.584
9100	3743	1	000728886	9100-051	G 09	0.347	52.75	Spy4H	0.1776	TR0910003743	#NAME?	$C_{37}H_{45}N_3O_4$	595.779

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID	Structure		
9100	812	1	000726195	9100-011	D 03	0.339	52.70	Spy4H	0.1776	TR0910000812	#NAME? 	$C_{31}H_{35}FN_2O_5$	534.625
9100	2196	1	000727339	9100-031	D 06	0.271	52.69	Spy4H	0.1776	TR0910002196	#NAME? 	$C_{31}H_{35}N_3O_5$	529.633
9100	2220	1	000727363	9100-031	D 09	0.269	52.69	Spy4H	0.1776	TR0910002220	#NAME? 	$C_{36}H_{44}N_4O_3$	580.769
9100	2437	1	000727580	9100-035	E 06	0.261	52.63	Spy4H	0.1776	TR0910002437	#NAME? 	$C_{27}H_{28}N_2O_4$	444.528

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID				Structure
9100	2757	1	000727900	9100-039	E 06	0.359	52.61	Spy4H	0.1776	TR0910002757	#NAME?	$C_{26} H_{25} Cl N_2 O_5$	480.945	
9100	2396	1	000727539	9100-033	D 11	0.334	52.60	Spy4H	0.1776	TR0910002396	#NAME?	$C_{29} H_{30} N_2 O_5$	486.565	
9100	229	1	000725612	9100-003	E 10	0.266	52.55	Spy4H	0.1776	TR0910000229	#NAME?	$C_{27} H_{32} Br N_3 O_3$	526.472	
9100	2604	1	000727747	9100-037	D 07	0 267	52.55	Spy4H	0 1776	TR0910002604	#NAME?	$C_{32} H_{33} Cl N_4 O_3$	557.091	

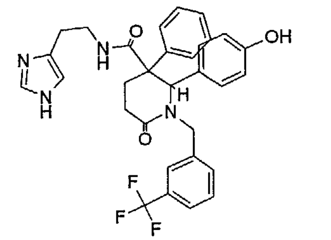
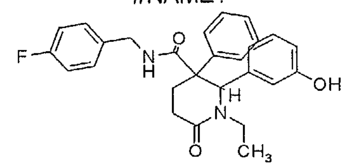
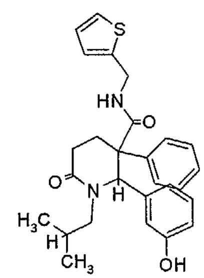
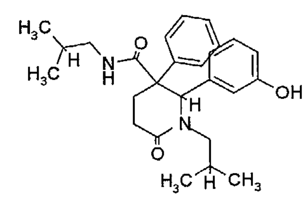
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2614	1	000727757	9100-037	F 08	0.317	52.55	Spy4H	0.1776	TR0910002614	#NAME?	$C_{33}H_{35}ClN_4O_3$	571.117
9100	3701	1	000728844	9100-051	E 04	0.418	52.44	Spy4H	0.1776	TR0910003701	#NAME?	$C_{31}H_{42}N_2O_3$	490.684
9100	3726	1	000728869	9100-051	F 07	0.275	52.44	Spy4H	0.1776	TR0910003726		$C_{32}H_{35}N_3O_4$	525.646

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3755	1	000728898	9100-051	C 11	0.294	52.44	Spy4H	0.1776	TR0910003755	#NAME?	$C_{35}H_{41}N_3O_4$	567.726
9100	1021	1	000726404	9100-013	E 09	0.399	52.37	Spy4H	0.1776	TR0910001021	#NAME?	$C_{29}H_{40}N_2O_3$	464.646
9100	1027	1	000726410	9100-013	C 10	0.28	52.37	Spy4H	0.1776	TR0910001027	#NAME?	$C_{27}H_{36}N_2O_4$	452.591

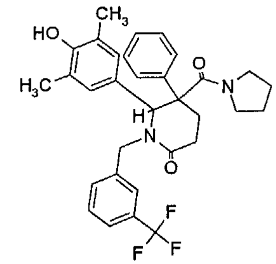
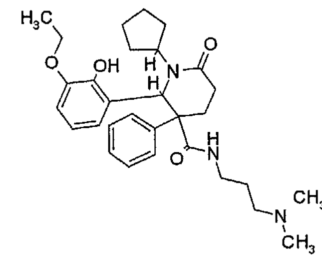
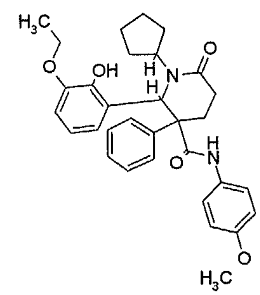
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	694	1	000726077	9100-009	F 08	0.285	52.36	Spy4H	0.1776	TR0910000694	#NAME?	$C_{34}H_{35}F_3N_4O_3$	604.669
9100	579	1	000725962	9100-008	C 04	0.261	52.35	Spy4H	0.1776	TR0910000579	#NAME?	$C_{27}H_{37}N_3O_3$	451.607
9100	603	1	000725986	9100-008	C 07	0.269	52.35	Spy4H	0.1776	TR0910000603	#NAME?	$C_{25}H_{30}N_2O_3$	406.523
9100	4123	1	000729266	9100-057	C 07	0.289	52.30	Spy4H	0.1776	TR0910004123	#NAME?	$C_{36}H_{43}N_3O_3$	565.754

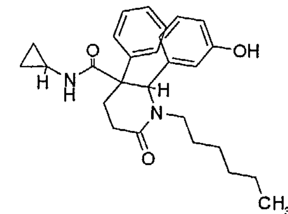
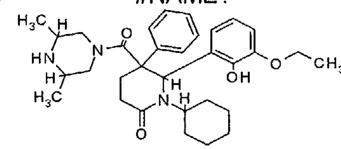
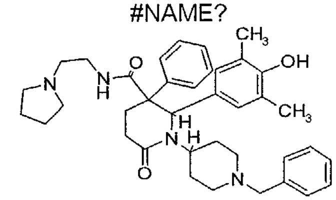
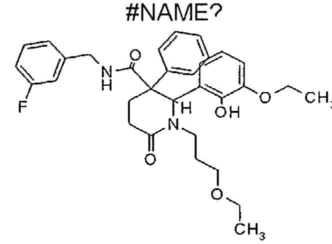
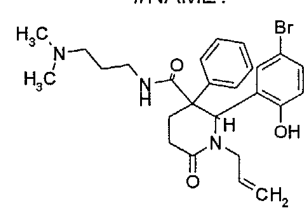
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	235	1	000725618	9100-003	C 11	0.485	52.25	Spy4H	0.1776	TR0910000235	#NAME?	$C_{27}H_{31}BrN_2O_3$	511.457
9100	820	1	000726203	9100-011	D 04	0.272	52.16	Spy4H	0.1776	TR0910000820	#NAME?	$C_{30}H_{41}N_3O_5$	523.67
9100	841	1	000726224	9100-011	A 07	0.354	52.16	Spy4H	0.1776	TR0910000841	#NAME?	$C_{31}H_{32}ClN_3O_4$	546.064
9100	872	1	000726255	9100-011	H 10	0.406	52.16	Spy4H	0.1776	TR0910000872	#NAME?	$C_{29}H_{31}ClN_2O_3$	491.028

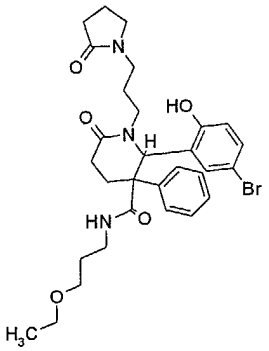
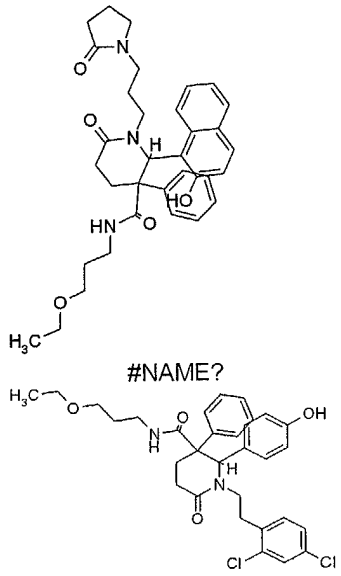
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3740	1	000728883	9100-051	D 09	0.275	52.14	Spy4H	0.1776	TR0910003740	#NAME?	$C_{35}H_{42}N_4O_4$	582.741
9100	580	1	000725963	9100-008	D 04	0.263	52.06	Spy4H	0.1776	TR0910000580	#NAME?	$C_{28}H_{37}N_3O_3$	463.618
9100	604	1	000725987	9100-008	D 07	0.261	52.06	Spy4H	0.1776	TR0910000604	#NAME?	$C_{26}H_{30}N_4O_3$	446.548
9100	707	1	000726090	9100-009	C 10	0.306	52.02	Spy4H	0.1776	TR0910000707	#NAME?	$C_{31}H_{33}F_3N_2O_4$	554.606

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	4084	1	000729227	9100-057	D 02	0.264	52.02	Spy4H	0.1776	TR0910004084	#NAME? 	$C_{31}H_{29}F_3N_4O_3$	562.589
9100	733	1	000726116	9100-010	E 03	0.253	51.92	Spy4H	0.1776	TR0910000733	#NAME? 	$C_{27}H_{27}FN_2O_3$	446.519
9100	578	1	000725961	9100-008	B 04	0.334	51.77	Spy4H	0.1776	TR0910000578	#NAME? 	$C_{27}H_{30}N_2O_3S$	462.611
9100	586	1	000725969	9100-008	B 05	0.301	51.77	Spy4H	0.1776	TR0910000586	#NAME? 	$C_{26}H_{34}N_2O_3$	422.566

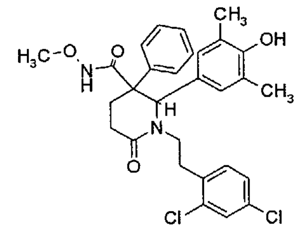
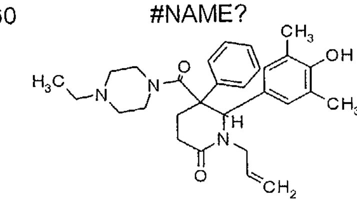
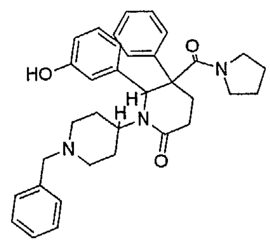
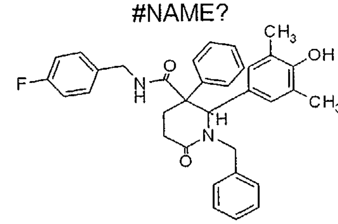
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	628	1	000726011	9100-008	D 10	0.263	51.77	Spy4H	0.1776	TR0910000628	#NAME?	$C_{25}H_{32}N_2O_4$	424.538
9100	630	1	000726013	9100-008	F 10	0.264	51.77	Spy4H	0.1776	TR0910000630	#NAME?	$C_{24}H_{26}N_2O_3$	390.48
9100	2977	1	000728120	9100-042	A 04	0.341	51.75	Spy4H	0.1776	TR0910002977	#NAME?	$C_{28}H_{28}Cl_2N_2O_4$	527 445
9100	1695	1	000726838	9100-023	G 03	0.442	51.74	Spy4H	0.1776	TR0910001695	#NAME?	$C_{25}H_{29}BrN_2O_3$	485.419

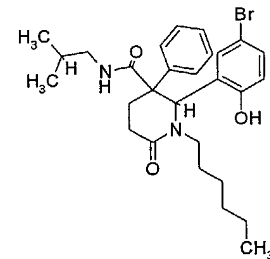
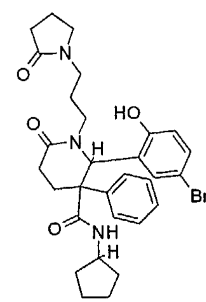
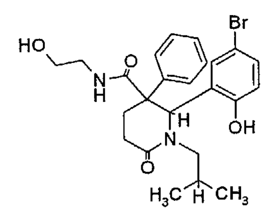
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	683	1	000726066	9100-009	C 07	0.546	51.69	Spy4H	0.1776	TR0910000683	#NAME?	$C_{32}H_{33}F_{3}N_{2}O_{3}$	550.618
													
9100	1939	1	000727082	9100-028	C 04	0.287	51.58	Spy4H	0.1776	TR0910001939	#NAME?	$C_{30}H_{41}N_{3}O_{4}$	507.671
													
9100	1956	1	000727099	9100-028	D 06	0.29	51.58	Spy4H	0.1776	TR0910001956	#NAME?	$C_{32}H_{36}N_{2}O_{5}$	528.645
													

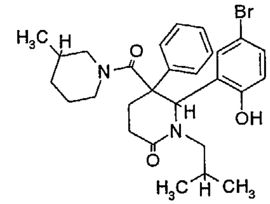
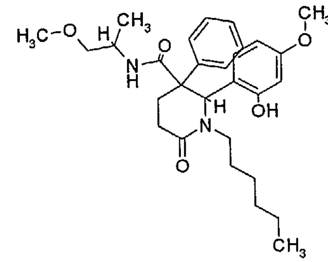
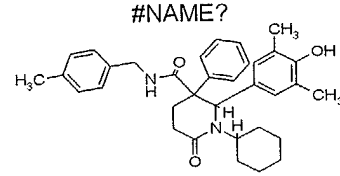
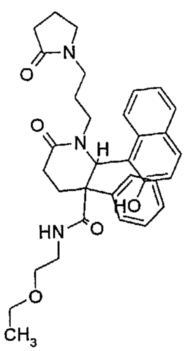
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1015	1	000726398	9100-013	G 08	0.352	51.56	Spy4H	0.1776	TR0910001015	#NAME? 	$C_{27}H_{34}N_2O_3$	434.577
9100	2349	1	000727492	9100-033	E 05	0.299	51.48	Spy4H	0.1776	TR0910002349	#NAME? 	$C_{32}H_{43}N_3O_4$	533.709
9100	4122	1	000729265	9100-057	B 07	0.273	51.46	Spy4H	0.1776	TR0910004122	#NAME? 	$C_{38}H_{48}N_4O_3$	608.822
9100	2532	1	000727675	9100-036	D 08	0.323	51.44	Spy4H	0.1776	TR0910002532	#NAME? 	$C_{32}H_{37}FN_2O_5$	548.651
9100	219	1	000725602	9100-003	C 09	0.265	51.33	Spy4H	0.1776	TR0910000219	#NAME? 	$C_{26}H_{32}BrN_3O_3$	514.461

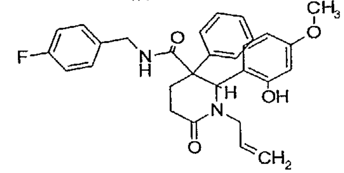
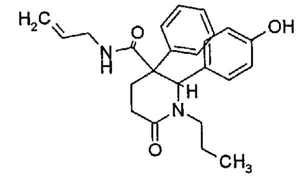
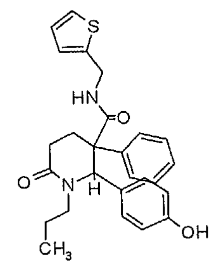
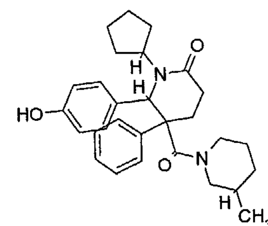
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	982	1	000726365	9100-013	F 04	0.28	51.29	Spy4H	0.1776	TR0910000982	#NAME?	$C_{30}H_{38}BrN_3O_5$	600.55
9100	3742	1	000728885	9100-051	F 09	0.276	51.22	Spy4H	0.1776	TR0910003742	 #NAME?	$C_{34}H_{41}N_3O_5$	571.714
9100	2982	1	000728125	9100-042	F 04	0.438	51.21	Spy4H	0.1776	TR0910002982	 #NAME?	$C_{31}H_{34}Cl_2N_2O_4$	569.526

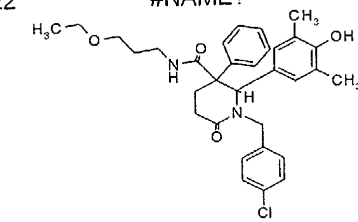
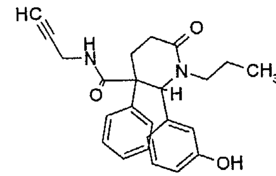
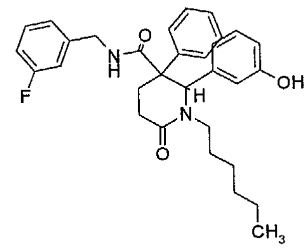
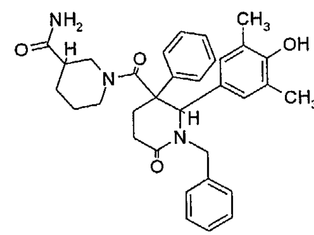
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1758	1	000726901	9100-023	F 11	0.298	51.20	Spy4H	0.1776	TR0910001758	#NAME?	$C_{31}H_{34}N_2O_4$	498.62
9100	2365	1	000727508	9100-033	E 07	0.34	51.19	Spy4H	0 1776	TR0910002365	#NAME?	$C_{27}H_{32}N_2O_4$	448.56
9100	588	1	000725971	9100-008	D 05	0.267	51.19	Spy4H	0.1776	TR0910000588	#NAME?	$C_{26}H_{34}N_2O_4$	438.565
9100	620	1	000726003	9100-008	D 09	0.264	51.19	Spy4H	0.1776	TR0910000620	#NAME?	$C_{27}H_{35}N_3O_3$	449.591

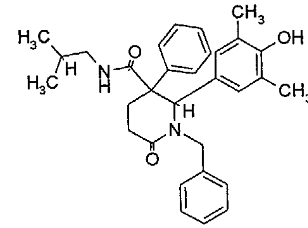
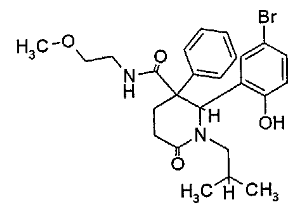
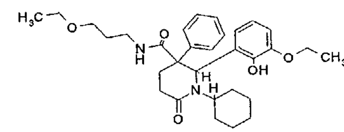
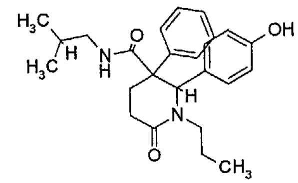
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2519	1	000727662	9100-036	G 06	0.383	51.17	Spy4H	0.1776	TR0910002519	#NAME? 	$C_{29}H_{30}Cl_2N_2O_4$	541.472
9100	1060	1	000726443	9100-014	D 04	0.269	51.06	Spy4H	0.1776	TR0910001060	#NAME? 	$C_{29}H_{37}N_3O_3$	475.629
9100	2203	1	000727346	9100-031	C 07	0.277	51.06	Spy4H	0.1776	TR0910002203	#NAME? 	$C_{34}H_{39}N_3O_3$	537.7
9100	2413	1	000727556	9100-035	E 03	0.49	51.02	Spy4H	0.1776	TR0910002413	#NAME? 	$C_{34}H_{33}FN_2O_3$	536.644

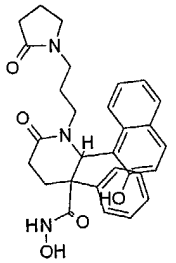
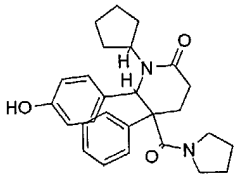
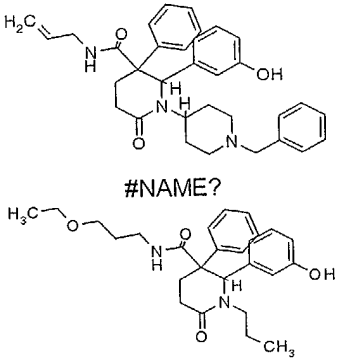
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2466	1	000727609	9100-035	B 10	0.394	51.02	Spy4H	0.1776	TR0910002466	#NAME?	$C_{28} H_{37} Br N_2 O_3$	529.515
													
9100	965	1	000726348	9100-013	E 02	0.337	51.02	Spy4H	0.1776	TR0910000965	#NAME?	$C_{30} H_{36} Br N_3 O_4$	582.535
													
9100	1697	1	000726840	9100-023	A 04	0.363	50.94	Spy4H	0.1776	TR0910001697	#NAME?	$C_{24} H_{29} Br N_2 O_4$	489.407
													

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1715	1	000726858	9100-023	C 06	0.557	50.94	Spy4H	0.1776	TR0910001715	#NAME? 	$C_{28}H_{35}BrN_2O_3$	527.5
9100	3033	1	000728176	9100-042	A 11	0.445	50.94	Spy4H	0.1776	TR0910003033	#NAME? 	$C_{29}H_{40}N_2O_5$	496.644
9100	3691	1	000728834	9100-051	C 03	0.457	50.92	Spy4H	0.1776	TR0910003691	#NAME? 	$C_{34}H_{40}N_2O_3$	524.701
9100	3748	1	000728891	9100-051	D 10	0.275	50.92	Spy4H	0.1776	TR0910003748	#NAME? 	$C_{33}H_{39}N_3O_5$	557.687

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2373	1	000727516	9100-033	E 08	0.351	50.91	Spy4H	0.1776	TR0910002373	#NAME? 	$C_{29}H_{29}FN_2O_4$	488.556
9100	606	1	000725989	9100-008	F 07	0.266	50.90	Spy4H	0.1776	TR0910000606	#NAME? 	$C_{24}H_{28}N_2O_3$	392.496
9100	618	1	000726001	9100-008	B 09	0.291	50.90	Spy4H	0.1776	TR0910000618	#NAME? 	$C_{26}H_{28}N_2O_3S$	448.584
9100	2795	1	000727938	9100-039	C 11	0.392	50.87	Spy4H	0.1776	TR0910002795	#NAME? 	$C_{29}H_{36}N_2O_3$	460.614

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2622	1	000727765	9100-037	F 09	0.377	50.83	Spy4H	0.1776	TR0910002622	#NAME? 	$C_{32} H_{37} Cl N_2 O_4$	549.107
9100	1110	1	000726493	9100-014	F 10	0.272	50.78	Spy4H	0.1776	TR0910001110	#NAME? 	$C_{24} H_{26} N_2 O_3$	390.48
9100	1012	1	000726395	9100-013	D 08	0.517	50.75	Spy4H	0.1776	TR0910001012	#NAME? 	$C_{31} H_{35} F N_2 O_3$	502.626
9100	2401	1	000727544	9100-035	A 02	0.33	50.70	Spy4H	0.1776	TR0910002401	#NAME? 	$C_{33} H_{37} N_3 O_4$	539.672

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2426	1	000727569	9100-035	B 05	0.324	50.70	Spy4H	0.1776	TR0910002426	#NAME? 	$C_{31} H_{36} N_2 O_3$	484.636
9100	1687	1	000726830	9100-023	G 02	0.338	50.67	Spy4H	0.1776	TR0910001687	#NAME? 	$C_{25} H_{31} Br N_2 O_4$	503.434
9100	2342	1	000727485	9100-033	F 04	0.32	50.63	Spy4H	0.1776	TR0910002342	#NAME? 	$C_{31} H_{42} N_2 O_5$	522.682
9100	626	1	000726009	9100-008	B 10	0.284	50.62	Spy4H	0.1776	TR0910000626	#NAME? 	$C_{25} H_{32} N_2 O_3$	408.539

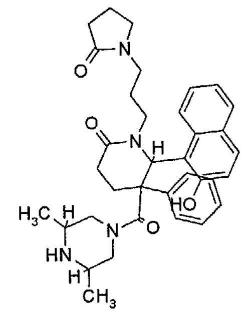
Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID				
9100	3757	1	000728900	9100-051	E 11	0.272	50.61	Spy4H	0.1776	TR0910003757		#NAME?	$C_{29}H_{31}N_3O_5$	501.58
9100	2763	1	000727906	9100-039	C 07	0.322	50.58	Spy4H	0.1776	TR0910002763		#NAME?	$C_{27}H_{32}N_2O_3$	432.561
9100	2206	1	000727349	9100-031	F 07	0.277	50.51	Spy4H	0.1776	TR0910002206		#NAME?	$C_{33}H_{37}N_3O_3$	523.673
9100	1102	1	000726485	9100-014	F 09	0.271	50.50	Spy4H	0.1776	TR0910001102		#NAME?	$C_{26}H_{34}N_2O_4$	438.565

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	2430	1	000727573	9100-035	F 05	0.288	50.38	Spy4H	0.1776	TR0910002430	#NAME?	$C_{30}H_{30}N_2O_3$	466.578
9100	717	1	000726100	9100-009	E 11	0.252	50.34	Spy4H	0.1776	TR0910000717	#NAME?	$C_{28}H_{27}F_3N_2O_4$	512.525
9100	2204	1	000727347	9100-031	D 07	0.278	50.24	Spy4H	0.1776	TR0910002204	#NAME?	$C_{35}H_{39}N_5O_3$	577.725
9100	2219	1	000727362	9100-031	C 09	0.282	50.24	Spy4H	0.1776	TR0910002219	#NAME?	$C_{35}H_{44}N_4O_3$	568.758

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1059	1	000726442	9100-014	C 04	0.273	50.21	Spy4H	0.1776	TR0910001059	#NAME?	$C_{28}H_{37}N_3O_3$	463.618
9100	1109	1	000726492	9100-014	E 10	0.273	50.21	Spy4H	0 1776	TR0910001109	#NAME?	$C_{27}H_{35}N_3O_3$	449.591
9100	1981	1	000727124	9100-028	E 09	0.283	50.21	Spy4H	0.1776	TR0910001981	#NAME?	$C_{28}H_{38}N_2O_4$	466.618
9100	974	1	000726357	9100-013	F 03	0.28	50.20	Spy4H	0.1776	TR0910000974		$C_{31}H_{36}BrN_5O_4$	622.56

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	1686	1	000726829	9100-023	F 02	0.427	50.13	Spy4H	0.1776	TR0910001686	#NAME?	$C_{25}H_{29}BrN_2O_3$	485.419
9100	2493	1	000727636	9100-036	E 03	0.532	50.10	Spy4H	0.1776	TR0910002493	#NAME?	$C_{35}H_{33}Cl_2FN_2O_3$	619.561
9100	587	1	000725970	9100-008	C 05	0.273	50.04	Spy4H	0.1776	TR0910000587	#NAME?	$C_{25}H_{32}N_2O_4$	424.538
9100	828	1	000726211	9100-011	D 05	0.28	50.00	Spy4H	0.1776	TR0910000828	#NAME?	$C_{28}H_{38}N_2O_6$	498.616

Library	Cmpd	Lot	ExtReg	Plate	Well	Raw Data	Assay Result	Assay	Conc mg/ml	LionID			
9100	3749	1	000728892	9100-051	E 10	0.28	50.00	Spy4H	0.1776	TR0910003749	#NAME?	$C_{35} H_{42} N_4 O_4$	582.741



EXAMPLE 4

Melanocortin Receptor Assay

[0124] This example describes methods for assaying binding to MC receptors.

[0125] All cell culture media and reagents are obtained from GibcoBRL (Gaithersburg MD), except for COSMIC CALF SERUM (HyClone; Logan UT). HEK 293 cell lines are transfected with the human MC receptors hMCR-1, hMCR-3, and hMCR-4 (Gantz et al., Biochem. Biophys. Res. Comm. 200:1214-1220 (1994); Gantz et al., J. Biol. Chem. 268:8246-8250 (1993); Gantz et al. J. Biol. Chem. 268:15174-15179 (1993); Haskell-Leuvano et al., Biochem. Biophys. Res. Comm. 204:1137-1142 (1994); each of which is incorporated herein by reference). Vectors for construction of an hMCR-5 expressing cell line are obtained, and a line of HEK 293 cells expressing hMCR-5 is constructed (Gantz, *supra*, 1994). hMCR-5 has been described previously (Franberg et al., Biochem. Biophys. Res. Commun. 236:489-492 (1997); Chowdhary et al., Cytogenet. Cell Genet. 68:1-2 (1995); Chowdhary et al., Cytogenet. Cell Genet. 68:79-81 (1995), each of which is incorporated herein by reference). HEK 293 cells are maintained in DMEM, 25 mM HEPES, 2 mM glutamine, non-essential amino acids, vitamins, sodium pyruvate, 10% COSMIC CALF SERUM, 100 units/ml penicillin, 100 µg/ml streptomycin and 0.2 mg/ml G418 to maintain selection.

[0126] Before assaying, cells are washed once with phosphate buffered saline ("PBS"; without Ca2+ and Mg2+), and stripped from the flasks using 0.25% trypsin and 0.5 mM EDTA. Cells are suspended in PBS, 10% COSMIC CALF SERUM and 1 mM CaCl2. Cell suspensions are prepared at a density of 2x104 cells/ml for HEK 293 cells expressing hMCR-3, hMCR-4 or hMCR-5, and 1x105 cells/ml for HEK 293 cells expressing hMCR-1. Suspensions are placed in a water bath and allowed to warm to 37°C for 1 hr.

[0127] Binding assays are performed in a total volume of 250 μl for HEK 293 cells. Control and test compounds are dissolved in distilled water. 125I-HP 467 (50,000 dpm) (2000 Ci/mmol) (custom labeled by Amersham; Arlington Heights IL) is prepared in 50 mM Tris, pH 7.4, 2 mg/ml BSA, 10 mM CaCl2, 5 mM MgCl2,

2 mM EDTA and added to each tube. To each tube is added 4x103 HEK 293 cells expressing hMCR-3, hMCR-4 or hMCR-5, or 2x104 cells expressing hMCR-1. Assays are incubated for 2.5 hr at 37°C.

[0128] GF/B filter plates are prepared by soaking for at least one hour in 5 mg/ml BSA and 10 mM CaCl2. Assays are filtered using a Brandel 96-well cell harvester (Brandel Inc.; Gaithersburg, MD). The filters are washed four times with cold 50 mM Tris, pH 7.4, and the filter plates dehydrated for 2 hr and 35 µl of MICROSCINT is added to each well. Filter plates are counted using a Packard Topcount (Packard Instrument Co.) and data analyzed using GraphPad PRISM v2.0 (GraphPad Software Inc.; San Diego CA) and Microsoft EXCEL v5.0a (Microsoft Corp.; Redmond WA).

[0129] To assay piperidine-3-carboxamide derivative compounds, binding assays are performed in duplicate in a 96 well format. HP 467 is prepared in 50 mM Tris, pH 7.4, and 125I-HP 467 is diluted to give 100,000 dpm per 50 µl. A piperidine-3-carboxamide derivative compound, is added to the well in 25 µl aliquots. A 25 µl aliquot of 125I-HP 467 is added to each well. A 0.2 ml aliquot of suspended cells is added to each well to give the cell numbers indicated above, and the cells are incubated at 37°C for 2.5 hr. Cells are harvested on GF/B filter plates as described above and counted.

EXAMPLE 5

Penile erection due to administration of a piperidine-3-carboxamide derivative compounds

[0130] Adult male rats are housed 2-3 per cage and are acclimated to the standard vivarium light cycle (12 hr. light, 12 hr. dark), rat chow and water for a least a week prior to testing. All experiments are performed between 9 a.m. and noon and rats are placed in cylindrical, clear plexiglass chambers during the 60 minute observation period. Mirrors are positioned below and to the sides of the chambers, to improve viewing.

[0131] Observations begin 10 minutes after an intraperitoneal injection of either saline or compound. An observer counts the number of grooming motions,

stretches, yawns and penile erections (spontaneously occurring, not elicited by genital grooming) and records them every 5 minutes, for a total of 60 minutes. The observer is unaware of the treatment and animals are tested once, with n=6 in each group. Values in the figures represent the group mean and standard error of the mean. HP 228 can be used as a positive control for penile erections. Significant differences between groups are determined by an overall analysis of variance and the Student Neunmann-Keuls post hoc test can be used to identify individual differences between groups (p £ 0.05).

[0132] Although the invention has been described with reference to the examples provided above, it should be understood that various modifications can be made by those skilled in the art without departing from the invention. Accordingly, the invention is set out in the following claims.